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VITELLOGENESIS IN INSECTS AND OTHER GROUPS – A REVIEW

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The eggs from oviparous organisms contain large amounts of vitellus, or yolk, which are utilized by the growing embryo. Vitellogenesis is the process of vitellus accumulation and involves massive heterosynthetic synthesis of the protein vitellogenin (Vg) and its deposition in the oocyte. This work summarizes data on Vg structure, synthesis, uptake by oocytes and its fate during embryogenesis. The hormonal control of vitellogenesis and its tissue, sex and temporal regulation are also discussed. Where it is available, data on structure and expression of Vg-coding genes are reviewed. Insect vitellogenesis is priorized although other oviparous animal groups outside insects are also treated.

Key words: hormonal control – insects – vitellin – vitellogenesis – vitellogenin – vitellogenin genes – vitellogenin synthesis

The embryonic development of oviparous animals occurs isolated from the maternal body. The egg should therefore contain all necessary supplies for the development of the embryo until eclosion. This supply is called vitellus, or yolk, and is composed of proteins, sugars and lipids, stored in an organized manner inside the egg.

Vitellogenesis is the period of rapid oocyte growth, when the vitellus deposition occurs (Pan et al., 1969; Hagedorn & Kunkel, 1979; Postlethwait & Giorgi, 1985). Vitellin (Vn) is the major protein of the vitellus in almost all of the organisms studied. Vitellin derives from vitellogenin (Vg), whose expression shows development, sexual, hormonal and tissue specificity.

Vitellogenin synthesis occurs in a short period of time and in many cases involves extensive cytological remodelling of structures of both the organ responsible for its synthesis (fat body) and uptake (ovary).

The physiology, endocrinology, cellular biology and biochemistry of Vg and vitellogenesis have been studied in great detail. Data concerning the genes coding for Vg are being used for the elucidation of its structure, the control mechanisms of its expression and the processes that govern its evolution.

This review summarizes the data needed to understand the basic aspects of insect vitellogenesis. Data and considerations of Vg structure, its synthesis and uptake, utilization during embryogenesis, the Vg coding genes and the hormonal control of its expression are treated separately. Several groups of oviparous animals outside insects will be also discussed.

VITELLOGENIN STRUCTURE

Table I contains information about Vg structure of different groups. Vitellogenins are phospholipoglycoproteins composed of different subunits that can be found as monomers or dimers with a native molecular weight (MW) in the range of 300-600 Kd. Vitellogenins of the higher diptera, with a native MW of 200 Kd, are an exception.

The phosphate groups present in Vg are generally either bound to serine or via phospholipids. More recently, phosphate groups were also found associated with mannose in Vg of *Rhodnius prolixus* (Masuda & Oliveira, 1985) and it seems that in Vg of the moth *Manduca sexta* a small portion of the phosphate is also associated with the carbohydrates (Osir et al., 1986b). The carbohydrates associated with Vg are of the high-mannose type in insects (Ng & Dain, 1976) and of the complex

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TABLE I

Structure of vitellogenin (Vg) and vitellin (Vn). The native and denatured molecular weights of Vg, Vg precursors and Vg subunits from different species are shown. Modifications such as glycosylation (G), phosphorylation (P) and the presence of lipids (L) in the Vg molecule are also indicated. (+) means that the corresponding modification has been detected but not quantified

Organism	Native MW (Kd)	Precursor (Kd)	Subunits (Kd)	Modification G	L	P	References
NEMATODE							
Caenorhabditis elegans			170 (A)	+			Klass et al., 1979
			170 (B)	+			Sharrock, 1983
		180	115,88	+			Sharrock, 1984
ECHINODERM							
Strongylocentrotus purpuratus	240(Vn)	195 (Vg)	180 (Vn)	+			Harrington & Easton, 1982 Shyu et al., 1986
POLYCHAETE							
Perinereis cultrifera	320; 530(Vg) 380 (Vn)	176	176(Vg) 98, 83, 22, 20, 16 (Vn)	5%	16%		Baert et al., 1984 Baert & Slomianny, 1987
Nereis virens	420		20.8, 13.5	+			Fischer & Schmitz, 1981 Baert et al., 1984
TICK							
Dermacentor andersoni	700; 4000 (VnA) 700; 8000 (VnB)		7 subunits	4.6%	7%	+	Boctor & Kamel, 1976
Ornithodoros moubata	300; 600 (Vg) 600 (Vn)	215, 210	215, 210, 160, 140, 125, 100 (Vg) + 64, 50 (Vn)	12.4%	7.6%		Chinzei et al., 1983
CRUSTACEAN							
Armadillidium vulgare	700, 620 540, 470		127, 90, 80	+			Suzuki, 1987
THYSANURA							
Thermobia domestica	430, 300, 240						Rousset et al., 1987
COCKROACH							
Blatella germanica		240	160, 102 (Vg) 102, 95, 50 (Vn)	+			Storella & Kunkel, 1979 Wojchowski et al., 1986
Leucophaea maderae	14S, 28S (Vn)	215	155, 112, 95, 92, 54 (Vg) 112, 90, 54 (Vn)	8.5%	6.9%	+	Dejmal & Brookes, 1972 Engelmann & Friedel, 1974 Della-Cioppa & Engelmann, 1987
Periplaneta americana	520 (17S, Vn)		170, 105, 92, 78 (Vn1) 105, 101, 60 (Vn2)				Storella et al., 1985
STICK INSECT							
Bacilus rossius			180-60 (5)				Giorgi et al., 1989
LOCUST							
Locusta migratoria	530-550 16,3-17S pI 6.9 (Vn)	265, 250	126, 117, 112, 104, 64, 54 (Vg) + 96, 57 (Vn)	13.6%	10%		Chen et al., 1976 Gellissen et al., 1976 Chen et al., 1978 Chen, 1980
CRICKET							
Ceutophilus sp.		~ 200 (2 Prec.)	165, 124, 118, 83	+			Bradley et al., 1987
Achaeta domesticus	352, 327 (Vg)		130, 97, 49, 47	+			Bradley & Edwards, 1978 Nicolaro & Bradley, 1980
HEMIPTERAN							
Triatoma proctracta	437 (Vn)						Mundall & Engelmann, 1977

cont.

Organism	Native MW (Kd)	Precursor (Kd)	Subunits (Kd)	Modification G	L	P	References
Rhodnius prolixus	260, 430 (Vg)	205, 190	159, 148, 53, 48	+	+	+	Chalaye, 1979 Masuda & Oliveira, 1985 Valle et al., 1987 Valle et al., 1992a
MOTH *Manduca sexta*	260 (Vg)		177, 47	3%	13%	+	Mundall & Law, 1977 Osir et al., 1986b
Philosamia cynthia	500 (Vn)				10%		Chino et al., 1976
Plodia interpunctella	462 (Vn1) 264 (Vn2)	>200	153, 147, 43 69, 33 (ovary)				Shirk et al., 1984
Hyalophora cecropia	15.9S (1 Vg) pI 5.7						Kunkel & Pan, 1976
Bombyx mori	420-440 (Vn) 13.5S	200 (180)	180, 42	3%	7.5%	+	Izumi et al., 1980 Izumi & Tomino, 1983 Zhu et al., 1986
LOWER DIPTERA *Aedes aegypti*	380 (Vg)	250	200, 65	6-10%	+	+	Hagedorn (pers. comm.) Raikhel, 1987 Bose & Raikhel, 1988 Raikhel et al., 1990
Culex pipiens fatigans	380 (Vn)		160, 82	+	+	+	Atlas et al., 1978
Rhyncosciara americana	500 (Vg)		211, 201, 70, 58	9.5%		+	Pereira & De Bianchi, 1983
HIGHER DIPTERA *Dacus oleae*			47, 49				Zongza & Dimitriadis, 1988
Musca domestica	2 Vn		54, 52, 51, 48, 46				De Bianchi, 1987
Calliphora vicina	210 (Vn)		49, 46 51, 49 (ovary)				Fourney et al., 1982
Stomoxys calcitrans			50.6-41.1 (6)				Chen et al., 1987
Sarcophaga bullata			56.1, 53.7, 50	+			Huybrechts & De Loof, 1982 Briers & Huybrechts, 1984
Drosophila melanogaster			46, 45, 44				Warren & Mahowald, 1979
COLEOPTERA *Coccinella septempunctata*	400 (Vn)		133, 130, 46, 43	+		+	Zhai et al., 1984
Leptinotarsa decemlineata	(2 Vg)		280, 271, 229, 50.5 (Vg1) 282, 271, 236, 226, 221, 48 (Vg2)	+	+		Peferoen et al., 1982
VERTEBRATE *Xenopus laevis*	460	210-220	121, 116, 111 (Lv1) 34, 31.5, 30.5 (Lv2) 34, 33 (phosvitin) 19, 13, 14 (phosvetes)	10-11%	12%	+	Wahli, 1988 Byrne et al., 1989
Gallus gallus	450-500	235-260	135, 105 (Lv1) 40, 30 (Lv2) 34, 28, 18, 15, 13 (phosvitin)	+		+	Protter et al., 1982 Byrne et al., 1989

type in vertebrates (Gottlieb & Wallace, 1982). In invertebrates the predominant sugars are mannose and N-acetylglycosamine, generally in the proportion of 4:1 (Dejmal & Brookes, 1972; Chinzei et al., 1983; Baert et al., 1984). The lipids associated with Vg are mainly di- and triglycerides, phosphatidylcholine, phosphatidylethanolamine and cholesterol (Hagedorn & Judson, 1972; Chen et al., 1976; Izumi et al., 1980; Baert et al., 1984). Furthermore, evidence has recently been obtained that *Aedes aegypti* Vg is submitted to sulfation in the Golgi complex during the maturation of the subunits (Dhadialla & Raikhel, 1990; Raikhel et al., 1990).

Vitellogenins contain several subunits in a wide range of MW and the stoichiometric relationship among these subunits is often difficult to determine. In some cases, polypeptides described as part of Vg are actually derivatives of the proteolytic processing of this molecule. This can be the consequence of a failure to control degradation during sample preparation (Chen et al., 1976, 1978; Baert et al., 1984; Storella et al., 1985; Brookes, 1986; Della-Cioppa & Engelmann, 1987; Borovsky & Whitney, 1987).

In the majority of insects Vg has subunits in the ranges of 150-200 and 50-60 Kd, derived from precursors with MW around 200 Kd. Interestingly, cleavage of these precursors can occur at alternative sites, generating subunits with both homologous and specific regions (Chen et al., 1978). The higher diptera are an exception since they have only subunits in the range of 50 Kd, which are synthesized as precursors of a slightly higher MW that loose only the signal peptide during secretion (Postlethwait & Kaschnitz, 1978; Brennan et al., 1980). Additionally, amino acid sequence comparisons among different Vgs showed no similarity between those from *Drosophila melanogaster* and from other organisms. Furthermore, evidence has been obtained of homology between *Drosophila* Vg (called yolk protein, YP, as stated below) and the triacylglycerl lipase family, a characteristic not shared by other Vgs (Terpstra & AB, 1988; Baker, 1988; Bownes et al., 1988).

Other female specific proteins secreted by fat bodies and accumulated by oocytes have been identified. This is the case of a 31 Kd protein called microvitellogenin found in *Hyalophora cecropia* (Kulakosky & Telfer, 1987) and in *M. sexta* (Kawooya et al., 1986; Wang et al., 1988) and of a 21 Kd female specific protein from *L. migratoria* (Zhang & Wyatt, 1990). In *A. aegypti* a 53 Kd vitellogenic carboxipeptidase synthesized by the fat body and sequestered by the oocytes has been recently described (Hays & Raikhel, 1990; Cho et al., 1991). In *Bombyx mori* a group of related hemolymph proteins, called "30 Kd proteins", are present in significant amounts inside the oocytes (Zhu et al., 1986; Sakai et al., 1988). Additionally, proteins synthesized by the follicle cells and deposited in yolk bodies are known in some Lepidoptera, like the 70 Kd paravitellogenin from *H. cecropia* (Bast & Telfer, 1976; Raikhel & Dhadialla, 1992), the 72 Kd egg-specific protein (ESP) from *B. mori* (Irie & Yamashita, 1983; Zhu et al., 1986) and two follicle-specific proteins from *M. sexta* (Tsuchida et al., 1991). However, these proteins bear no relation to vitellogenin.

In other organisms Vgs are also synthesized as 200-250 Kd precursors (Table I) and, in the case of vertebrates, the cleavage products are called lipovitellins (Lv) and phosvitins. There are two different Lv, with 110-120 Kd (Lv1) and with 30-40 Kd (Lv2) (Table I). The lipovitellins are lipoproteins with 20% lipids and low contents of phosphorus (0.5%) and sugars (0.3%). Phosvitins contitute a Vg domain which is absent from Vg of invertebrates. They show a low lipid content (0.4%), 10-11% of carbohydrates and approximately 50% of serine residues, the majority of which is phosphorylated (Tata & Smith, 1979). In *Xenopus laevis* an additional cleavage in the phosvitin domain of one of the Vg variants gives rise to smaller phosphoproteins, called phosvetes (Wahli, 1988). Inside the egg Lv and phosvitins are associated in crystalline complexes with high affinity for calcium (Tata & Smith, 1979).

It is believed that phosvitin is related to the bone formation of developing vertebrates, which require more phosphate and calcium than invertebrates (Wahli, 1988). Indications that phosvitin is evolving more rapidly than the rest of Vg and that the phosvitin evolution occurs through the expansion of serine containing regions (Byrne et al., 1989) corroborate this hypothesis.

The organization of Vg derivatives in vertebrates is NH2-Lv1-phosvitin-Lv2-COOH (Gerber-Huber et al., 1987; Van het Schip et

al., 1987a). In *Locusta migratoria* and *R. prolixus* the large Vg subunits (in the range of 150 Kd) are thought to occupy the C-terminal position in the Vg precursor (Wyatt et al., 1984b; Valle et al., 1992b).

Regions of homology have been found between Vg and von Willebrand factor, a glycoprotein that participates in the blood clotting of vertebrates. In this case, comparison with Vg led to the identification of an extra duplication event in the evolution of the cysteine rich D regions of von Willebrand factor (Byrne et al., 1989). Regions of homology have also been found between vertebrate and *Caenorhabdits elegans* Vg and the human B100-apolipoprotein, an LDL fraction component (Baker, 1988; Byrne et al., 1989). Additionally, homology has been found between *D. melanogaster* YP and lipoprotein lipases (Baker, 1988; Bownes et al., 1988; Terpstra & AB, 1988). These data, together with biological similarities among these proteins, led to the suggestion that Vgs are ancestors of B100-apolipoprotein, and that Vgs could exert biological functions other than merely being utilized as a yolk supply to the developing embryo (Baker, 1988).

SYNTHESIS AND UPTAKE OF VITELLOGENIN

Sites of Vg synthesis in different organisms are listed in Table II.

In the polychaetes Vg was thought to be autosynthesized, i.e., the oocytes, not integrated in gonads, would be the site of Vg synthesis. However, there is evidence in *Nereis virens* that some other somatic tissue synthesizes Vg (Fischer, 1979). Furthermore, recently the vitellogenin receptor in oocytes of *N. virens* was identified (Hafer et al., 1992). The vitellus heterosynthetic origin was also confirmed in the polychaete *Perinereis cultrifera*, where Vg synthesis by the coelomocytes was detected (Baert & Slomianny, 1987).

The fat body, equivalent to the vertebrate liver, is the exclusive site of Vg synthesis in the majority of the insects. In some coleoptera and higher diptera the ovary is an additional site of Vg synthesis (Table II). In the latter group therefore the term "yolk polypeptide" (YP) has been proposed because Vg is by definition, synthesized exclusively by fat bodies (Bownes, 1982).

In the cyclorrhaphan diptera, where the major YP synthesis occurs in the fat bodies, an alternating synthesis by the fat body and ovaries can occur during each vitellogenic cycle (De Bianchi et al., 1985; Zongza & Dimitriadis, 1988). On the other hand, in some higher dipteran species the ovary can be the principal or exclusive site of Vg synthesis (Chen et al., 1987; De Bianchi, 1987). In the coleoptera only a small amount of the total Vg found in the oocytes may be synthesized in the ovary (Zhai et al., 1984; Peferoen & De Loof, 1986).

In ticks and crustaceans Vg synthesis occurs in the fat body. However, the ovary is an additional site of Vg synthesis in the isopod *Porcellio dilatatus* (Table II) where the peaks of Vg synthesis by both organs do not occur at the same time (Souty, 1983).

During the vitellogenesis of insects the cells of the fat body undergo certain changes by which they are converted from lipid and glycogen storage cells to cells with a massive protein synthesis. Cytological studies of fat bodies of vitellogenic insects have been done mainly with *L. migratoria* (Chen et al., 1976; Rinterknecht & Roussel, 1978; Couble et al., 1979) and *A. aegypti* (Raikhel & Lea, 1983, 1987; Raikhel, 1987), although other insects have also been analysed, like the hemipteran *R. prolixus* (Chalaye et al., 1983) and the stick insect *Bacillus rossius* (Giorgi et al., 1989).

Ultrastructural and immunocytochemistry studies, carried mainly with *A. aegypti* (Raikhel & Lea, 1983; Raikhel, 1987), defined three distinctive phases in the fat body cells, during each oogenesis cycle: 1) the previtellogenic phase, in which the cells have large lipid inclusions, much glycogen and a contracted nucleus; 2) the vitellogenic phase, characterized by abundant rough endoplasmic reticulum and Golgi apparatus, large nucleus and multilobed nucleolus and 3) termination phase, when abundant lysosomes are present.

In *A. aegypti* the maximum intensity of Vg synthesis is attained 27 hours after the blood meal. The Vg synthesis then declines rapidly due to the action of lysosomes. Endoplasmic reticulum and Golgi complexes are degraded in two steps, that consist of the formation of a prelysosome and its fusion with a primary or secondary lysosome. The mature Vg-containing secretory granules, on the other hand, fuse with lysosomes directly (Raikhel, 1986a, b). These events are intense and precisely coordi-

TABLE II

Sites of vitellogenin synthesis

Organism	Site of synthesis	References
NEMATODE		
Caenorhabditis elegans	intestine (32 cells)	Kimble & Sharrock, 1983
ECHINODERM		
Strongylocentrotus purpuratus	intestine and gonads	Shyu et al., 1986
POLYCHAETE		
Perinereis cultrifera	celomocytes	Baert & Slomianny, 1987
Nereis virens	maybe somatic tissue	Fischer, 1979
TICK		
Ornithodoros moubata	fat body	Chinzei & Yano, 1985
CRUSTACEA		
Porcellio dilatatus	fat body and ovary	Picaud & Souty, 1980 Souty, 1983
COCKROACH		
Blatella germanica	fat body	Wojchowski et al., 1986
Leucophaea maderae	fat body	Brookes, 1986 Della-Cioppa & Engelmann, 1987
STICK INSECT		
Bacillus rossius	fat body	Giorgi et al., 1989
LOCUST		
Locusta migratoria	fat body	Couble et al., 1979
CRICKET		
Ceutophilus sp	fat body	Bradley et al., 1987
Achaeta domesticus	fat body	Chang & Bradley, 1983
HEMIPTERA		
Rhodnius prolixus	fat body	Valle et al., 1992a
MOTH		
Manduca sexta	fat body	Wang et al., 1988
Plodia interpunctella	fat body	Shirk et al., 1984
Hyalophora cecropia	fat body	Pan et al., 1969
LOWER DIPTERA		
Aedes aegypti	fat body	Hagedorn & Judson, 1972
Rhyncosciara americana	fat body	Pereira & De Bianchi, 1983
HIGHER DIPTERA		
Dacus oleae	fat body and ovary	Zongza & Dimitriadis, 1988
Musca domestica	fat body and ovary	De Bianchi et al., 1985
Calliphora vicina	fat body and ovary	Fourney et al., 1982
Stomoxys calcitrans	ovary	Chen et al., 1987
Sarcophaga bullata	fat body	Cardoen et al., 1988
Drosophila melanogaster	fat body and ovary	Kambysellis, 1977 Postlethwait et al., 1980
COLEOPTERA		
Coccinella septempunctata	fat body and ovary	Zhai et al., 1984
Leptinotarsa decemlineata	fat body and ovary	Peferoen & De Loof, 1986
VERTEBRATES		
Xenopus laevis	liver	Tata & Smith, 1979
Gallus gallus	liver	Tata & Smith, 1979

nated. Maximal activity of lysosomal enzimes have been detected at 30 hours after the blood meal (Raikhel, 1986b). In an attempt to study the regulation of the lysosomal activity in the fat body, the lysosomal enzime catepsin D has been recently purified and characterized (Raikhel et al., 1990).

In insects, the proteolytic processing of the Vg precursors occurs inside the fat bodies whereas in polichaetes, echinoderms and vertebrates it occurs only after uptake of the precursors by the oocytes. However, some variations can occur, e.g. the cleavage of the 180 Kd Vg precursor in the body cavity of *Caenorhabditis elegans* (Sharrock, 1984). Vitellogenin processing in the fat body and additional processing after oocyte uptake can occur in ticks (*Ornithodoros moubata*, Chinzei et al., 1983), cockroaches (*Blatella germanica*, Wojchowski et al., 1986) and locusts (*L. migratoria*, Chen, 1980). In the case of the cockroach *Leucophaea maderae* its is not yet clear whether the proteolysis occurs inside the oocytes (Brookes, 1986; Della-Cioppa & Engelmann, 1987).

In some insects all Vg subunits are glycosylated, e.g. in the cockroach *B. germanica* (Wojchowski et al., 1986), in the lower diptera *A. aegypti* (Raikhel, 1987) and *R. americana* (De Bianchi et al., 1982) and in the coleopteran *Coccinella septempunctata* (Zhai et al., 1984). On the other hand, in the moth *M. sexta* Vg only the larger subunit is glycosylated (Mundall & Law, 1979). In this species it has also been demonstrated that the smaller subunit is localized inside the native protein (Osir et al., 1986b). The distribution of differently processed oligosaccharides is thought to be species-characteristic (Nordin et al., 1984).

Vitellogenin precursor cleavage inside the fat body is subsequent to the glycosylation and/or phosphorylation processes in the cockroaches *B. germanica* (Wojchowski et al., 1986) and *L. maderae* (Della-Cioppa & Engelmann, 1987). Glycosylation is essential for the processing and secretion of Vg in *B. germanica* (Wojchowski et al., 1986) but not in the toad *X. laevis* (Gottlieb & Wallace, 1982). In contrast, deglycosylation of Vg from *M. sexta* does not alter significantly its uptake by the oocytes (Osir et al., 1986a).

In *A. aegypti* glycosylation occurs cotranslationally while cleavage and phosphorylation of Vg subunits are subsequent processes (Raikhel, 1987; Bose & Raikhel, 1988; Raikhel et al., 1990). If glycosylation is blocked by tunicamycin, *A. aegypti* pre-Vg is cleaved into its subunits but it is not phosphorylated and further processing and secretion are prevented (Dhadialla & Raikhel, 1990). Monoclonal antibodies specific to each of the *A. aegypti* Vg subunits were developed that recognize different steps on the Vg secretory pathways (Raikhel et al., 1986). These antibodies were used to confirm that *A. aegypti* Vg subunits originate from a common precursor and that processing, secretion and internalization of both subunits occur simultaneously (Raikhel & Lea, 1987; Bose & Raikhel, 1988). Recently it was shown that after cleavage, *Aedes* Vg subunits undergo additional maturation and that sulfation of these molecules in the Golgi complex is probably involved in this process (Dhadialla & Raikhel, 1990).

Vitellogenin from the silkworm *B. mori* is phosphorylated in the fat body and additional phosphorylation occurs in the ovary. In this species inhibition of protein synthesis blocks Vg secretion but not Vg phosphorylation (Takahashi, 1987). Chicken Vg is found in the blood as a phosphoglycoprotein, but in the hepatocytes it occurs mainly as a non-glycosylated and non-phosphorylated precursor, suggesting that glycosylation and phosphorylation occur immediately before secretion (Protter et al., 1982).

Vitellin accounts for 70-90% of the total protein in invertebrate eggs, with exception of *B. mori*, where it makes up only 30% of the total protein. In this species ESP and the "30 Kd proteins" make up 20-25% and 35% of the protein vitellus, respectively (Irie & Yamashita, 1980; Zhu et al., 1986).

Endocytosis of Vg by oocytes is selective and receptor-mediated. Analysis of this process in *A. aegypti* led to the first description of coated pits and coated vesicles, when it was verified that vitellus deposition is related to a 15-fold increase in the number of invaginations in the oocyte surface (Roth & Porter, 1964). Immunocytochemistry experiments confirmed that Vg binds mainly to microdomains at the base of oocyte microvilli, in regions with electrondense glycocalix, intracelularly coated with clathrin (Raikhel, 1984).

Evidences for the existence of a Vg receptor in the oocytes were found in several organ-

isms, like *N. virens* (Hafer et al., 1992), *R. prolixus* (Oliveira et al., 1986), *Nauphoeta cinerea* (Konig & Lanzrein, 1985; Indrasith et al., 1990), *L. migratoria* (Rohrkasten & Ferenz, 1986a, b; Rohrkasten et al., 1989), *M. sexta* (Osir & Law, 1986), *A. aegypti* (Koller et al., 1989; Raikhel et al., 1990; Dhadialla et al., 1992) and *X. laevis* (Opresko & Wiley, 1987). In *A. aegypti* phosphorylation of Vg is essential for its binding to the receptor (Dhadialla et al., 1992).

There is evidence of structural homology between locust and chicken Vg receptors. Structural identity as well as functional relationship among Vg receptors from anelids (*N. virens*) and locusts (*L. migratoria* and *S. gregaria*) has also been demonstrated (Hafer et al., 1992). On the other hand, *A. aegypti* Vg receptor does not exhibit structural homology to chicken or locust Vg receptors (Dhadialla et al., 1992). The chicken Vg receptor is able to bind the mammalian apoprotein E, apparently at the same recognition site as Vg. It has been suggested that Vn could be the oviparous protein equivalent to the apoprotein E (Steyrer et al., 1990).

Once in the oocyte, Vg is rapidly dissociated from the receptor and transported to endosomes. The fusion of these endosomes yields organelles called yolk bodies which are specialized in long-term storage and where the protein may be crystallized (Raikhel, 1984). Otherwise, proteins which are non-specifically internalized are accumulated in vesicles and shifted to the lysosomal system (Storella & Kunkel, 1979; Raikhel & Lea, 1986). Uptake and storage of yolk proteins by insect oocytes have been recently reviewed in great detail (Raikhel & Dhadialla, 1992).

UTILIZATION OF YOLK PROTEINS DURING EMBRYOGENESIS

Embryonic development consists of an initial phase of embryonic differentiation followed by larval differentiation inside the egg. In the initial phase Vn is not significantly utilized, being dispersed throughout the egg. Later Vn segregates to the embryonic intestine, where it is more intensely degraded, during the larval differentiation phase (Storella & Kunkel, 1979; Irie & Yamashita, 1980; Bownes, 1982; Storella et al., 1985; Oliveira et al., 1989). At the time of eclosion larvae of several insects still have varying amounts of Vn (Perassi, 1973; Irie & Yamashita, 1980; Sharrock, 1983; Zhu et al., 1986; Oliveira et al., 1989).

Analysis of the proteolytic processes occurring during embryogenesis resulted in the identification of proteases and proteolytic inhibitors in a variety of organisms (Indrasith et al., 1988; Kageyama & Takahashi, 1990). In *Rana pipiens* trypsin and chymotrypsin inhibitors have been identified that are integral parts of lipovitellin, one of the Vg subunits. This led to the speculation that yolk proteins could exert a dynamic role on the development control, a proposal that awaits further investigation (Salisburry et al., 1980).

Many insects have more than one Vn, and they can be differentially sequestered, being localized in distinct regions inside the oocyte, like in the cricket *A. domesticus* (Nicolaro & Bradley, 1980). It has also been observed that distinctive Vn molecules can be utilized at different rates during embryogenesis (in the stick insect *Carausius morosus,* Masetti & Giorgi, 1989; in the cockroach *P. americana,* Storella et al., 1985). In *R. prolixus* polypeptides derived from Vn cleavage remain in the same macromolecular complex, although different subunits decline with distinct ratios (Oliveira et al., 1989).

Vitellin makes up only 30% of the total egg proteins in *B. mori* (Irie & Yamashita, 1980; Zhu et al., 1986). The transplantation of ovaries into male larvae resulted in oocyte development without Vn, thus raising the question whether Vn is essential for the embryonic development. After induction of parthenogenesis, eclosion and larval development occurred normally in a certain number of the oocytes and some larvae even reached maturity (Yamashita & Irie, 1980). During *B. mori* embryonic differentiation (i.e. before the larvae formation inside the eggs), ESP is utilized rapidly and completely (Zhu et al., 1986) and seems to be the only protein to decline (Irie & Yamashita, 1980).

The egg specific proteins that have been observed in variable amounts in other moths (*H. cecropia,* Bast & Telfer, 1976; *Plodia interpunctella,* Shirk et al., 1984; *B. mori,* Zhu et al., 1986; *M. sexta,* Tsuchida, 1991) are supposed to be the major nutrient source during embryogenesis in Lepidoptera, since they are the first to be consumed (Shirk et al., 1984).

TABLE III

Vitellogenin mRNAs and genes. Vitellogenin mRNA size and *vit* genes size, number and location are indicated. The vitellogenin subunits of the nematode *Caenorhabditis elegans* coded by each *vit* gene are in brackets

Organism	mRNA (Kb)	Genes	Location	References
NEMATODE				
Caenorhabditis elegans	5.1	vit1 (pseudogene)	X chromosome	Blumenthal et al., 1984
		vit2 (170B)	X chromosome	Spieth & Blumenthal, 1985
		vit3-4-5 (170A)	X chromosome	
		vit6 (180)	autosomal	
ECHINODERM				
Strongylocentrotus purpuratus	5.1	1 vit (19Kb)		Shyu et al., 1986 Shyu et al., 1987
LOCUST				
Locusta migratoria	7.1 (31S)	VgA (12Kb) VgB (10.5Kb)	X chromosome	Applebaum et al., 1981 Bradfield & Wyatt, 1983 Locke et al., 1987
Schistocerca gregaria	6.3			Wyatt, 1988
HEMIPTERA				
Rhodnius prolixus	6.1			Valle et al., 1992b
LOWER DIPTERA				
Aedes aegypti	6.5	5 genes (4 cloned: A1, A2, B, C)		Gemmill et al., 1986 Hamblin et al., 1987
HIGHER DIPTERA				
Drosophila melanogaster	1.3	3 genes 1.35Kb (yp1-2-3)	X chromosome	Riddell et al., 1981 Barnett et al., 1980
VERTEBRATES				
Xenopus laevis	6.3	4 genes: A1 (21Kb), B1, A2 (16Kb), B2		Wahli & Dawid, 1980 Wahli et al., 1979
Gallus gallus		3 genes: Vtg1 (20,4Kb), 2 e 3		Van het Schip et al., 1987a Silva et al., 1989

GENES CODING FOR VITELLOGENIN AND YOLK PROTEINS

Vitellogenin-coding genes of the different species will be designated here as *vit* with exception of the Vg-genes in *D. melanogaster,* which are called *yp* in the literature. Data on the *vit* and *yp* genes are summarized in Table III.

Vitellogenin is coded by a small gene family in all species studied (2-6 copies per haploid genome). The echinoderm *S. purpuratus* is the unique exception known, in the sense it has only one copy of a *vit* gene (Shyu et al., 1987). It has been suggested that the products of the different *vit* gene copies could have different susceptibilities to hormonal stimulation or to degradation during the embryogenic process (Hamblin et al., 1987).

The *vit* genes are in general located on the X chromosome, comprise between 12 and 20 Kb in length and code for mRNAs in the range or 5-7 Kb (Table III). These transcripts (Vg mRNA) encode precursors of a MW around 200 Kd that are subsequently cleaved to generate the Vg subunits (Chen et al., 1976, 1978; Raikhel, 1987; Valle et al., 1992b). In this aspect the silkmoth *B. mori* is an exception, because its Vg subunits (180 and 42 Kd) are coded by distinct mRNAs (Izumi & Tomino, 1983).

In the nematode *C. elegans* the members of the subfamilies *vit 3-4-5* and *vit 1-2* (Table

III) have 95% of homology within the subfamilies, and the homology between both subfamilies is 70%. On the other hand, the homology between *vit 6* and *vit 1-5* is less than 50% (Spieth et al., 1985a). In another nematode of the same genus, *C. briggsae,* 5 genes *vit* have been identified, each one 85-90% homologous to the corresponding *vit* gene from *C. elegans* (Zucker-Aprison & Blumenthal, 1989). The nematode and vertebrate *vit* genes are homologous, mainly in the 5' region, thus suggesting a common origin.

L. migratoria vit genes (A and B) are polymorphic at the 3' region and show moderate homology to a 6.3 Kb mRNA from the locust *Schistocerca gregaria* (Bradfield & Wyatt, 1983; Locke et al., 1987).

The *vit* genes cloned from *A. aegypti* have been termed *A1, A2, B* and *C,* according to the homology levels among them, which is found mainly in the 3' region of the genes (Gemmill et al., 1986; Hamblin et al., 1987).

D. melanogaster yp genes, nonhomologous to other *vit* genes, are single copy, distinct, non-amplified and homologous to different YP mRNAs. However, they exhibit roughly 50% homology that can reach 73% in the C-terminal half (Barnett et al., 1980; Yan et al., 1987). *D. melanogaster yp 1* and *yp 2* genes have 1 intron while *yp 3* has 2 introns (Hovemann et al., 1981; Hovemann & Galler, 1982; Yan et al., 1987). The *yp 1* and *yp 2* genes have opposite orientations, with the 5' terminus 1221 bp apart (Riddell et al., 1981; Hovemann & Galler, 1982). The *yp 3* gene is located closer to the centromere, at about 1000 Kb from the other *yp* genes. In other *Drosophila* species analysed the *yp* genes have a similar arrangement, suggesting that maintainance of *yp* genes coupling during evolution may have some functional significance (Hatzopoulos & Kambysellis, 1987).

The *vit* genes from the toad *X. laevis* are classified in two groups, *A* and *B,* with 20% divergence. Each of these groups has two genes with 95% homology to each other (Wahli et al., 1979). In chicken the *vit 1* and *vit 2* genes code for abundant proteins whereas *vit 3* is less expressed (Protter et al., 1982; Silva et al., 1989). The comparison of *X. laevis* and chicken *vit* genes revealed a conservation in the position and number of the introns; however, a comparison of the exon sequences showed a variable degree of homology (Nardelli et al., 1987b).

The number of introns present in the *vit* genes from different invertebrate species has no obvious relation to their phylogenetic position. Therefore, the *vit* genes from the nematode *S. purpuratus* and the locust *L. migratoria* have several introns (Gerber-Huber et al., 1987; Shyu et al., 1987; Van het Schip et al., 1987a; Wyatt, 1988) while in *C. elegans* the size comparison between Vg mRNA and the *vit* genes points to the existence of few introns, a general characteristic in this species (Spieth et al., 1985b). Strikingly, it has been shown that the many introns present in vertebrate Vg (34 in chicken and frog) are related in position to those found in the nematode *C. elegans,* suggesting that the Vg gene is very ancient (Nardelli et al., 1987a). Recently the complete sequence of the boll weevil Vg gene was obtained (Trewitt et al., 1992). Protein sequence comparisons indicate that the *vit* gene of this coleopteran insect is a member of the nematode-vertebrate vitellogenin family.

The non-translated initial region of the *vit* genes comprises in general 9-28 bp, except in *S. purpuratus,* that comprises 99 bp (Shyu et al., 1987). The signal peptide coded by *vit* genes is homologous in the different species studied (Hovemann & Galler, 1982; Locke et al., 1987; Shyu et al., 1987; Byrne et al., 1989).

The 5' sequence of the *vit* gene transcripts studied is compatible with the formation of loops in the mRNA, suggesting inhibition of the translation initiation (Hung & Wensink, 1983; Zucker-Aprison & Blumenthal, 1989). Additionally, in some cases the signal peptide is coded by infrequent codons. It is believed that selection for the slow translation of the Vg mRNA initial region has occurred, ensuring an efficient interaction with the secretion apparatus (Spieth et al., 1985b; Yan et al., 1987).

Repetitive elements in introns and flanking DNA has been localized in the *vit* genes from *L. migratoria.* These elements, called *Lm1,* show characteristics reminiscent of the human *Alu family* (Wyatt, 1988). A repetitive element (CR1) has been localized at the 3' end of the chicken *vit* gene. This element has LTR characteristics and seems to be avian specific (Van het Schip et al., 1987b).

Analysis of *vit* genes promoters from some organisms are being conducted in order to find elements that could be responsible for the different kinds of control exerted on Vg expression, namely time-, sex- and stage-specificity or hormonal control.

In relation to the hormonal control, a sequence similar to the ERE (estrogen responsive element, 5'-GGTCANNNTGACC-3') has been localized in the sea-urchin *S. purpuratus* (Shyu et al., 1987) and in *D. melanogaster* (Hung & Wensink, 1983; Yan et al., 1987). The *L. migratoria* vit genes, which are regulated by juvenile hormone (JH), have blocks of homology in their promoter regions that seem to correspond to enhancer sequences responsible for tissue specificity or hormonal regulation. Two of these elements have a length of 12 bp and are related to elements found upstream of the *P. americana* oothecin gene, also stimulated by JH. One of these *L. migratoria* elements has an octanucleotide which is present in the *Drosophila* ERE (Locke et al., 1987).

The *X. laevis vit B1* gene promoter region has two imperfect ERE palindromes in a region called ERU (estrogen response unit). The regulatory capacity of each isolated ERE is very small or zero. Nonetheless, when ERU is present the receptor binds cooperatively (Martinez & Wahli, 1989). Furthermore, an heptamer known as *elegans box* has been localized near the vertebrate ERE. This element has been originally detected in the *C. elegans vit* gene promoter region (Spieth et al., 1985a). In *X. laevis* the *elegans box* increases the ERE basal activity, independently of the hormone. It has been suggested that this element is a conserved enhancer in estrogen regulated genes (Klein-Hitpass et al., 1986).

In insects, elements responsible for tissue specificity of expression are identified only in the case of the *D. melanogaster yp* genes. Either *yp 1* or *yp 2,* together with their respective promoter regions, were used in P-element mediated transformation of *D. melanogaster* germinal lineages. The transcripts of the introduced genes showed the original temporal and sexual expression patterns in the transformed flies. However, *yp 1* transcripts were found only in fat bodies and *yp 2* transcripts only in ovaries, suggesting that yp expression in different tissues is determined by distinct *cis* elements (Garabedian et al., 1985). Subsequently, the sex, stage and tissue specificity of Vg expression was assigned to a 125 bp segment localized in the region between *yp 1* and *yp 2.* This segment is functional in a heterologous promoter of an unrelated *Drosophila* gene, in different orientations or at different distances from the transcription initiation point. Therefore, this segment determines the *yp 1* expression pattern in the fat body and presumably has an enhancer function (Garabedian et al., 1986).

The differentiation of *D. melanogaster* is known to be controlled by various regulatory genes, arranged in hierarchical cascades (Baker, 1989; Wyatt, 1991). The sex determination regulatory genes are required for initiation and maintenance of sex-specific YP synthesis (Belote et al., 1985). Recent data showed a direct linkage between the regulatory cascade controlling somatic sexual diferentiation and some target genes, namely the *yp* genes (Burtis et al., 1991). This work evidenced binding of the products of one of the sex determination genes, *doublesex (dsx)* to the 125 bp enhancer element between *yp 1* and *yp 2.* It was suggested that this binding is related to the sex-specific expression of *yp* genes in *Drosophila.*

HORMONAL CONTROL OF VITELLOGENESIS

Vitellogenesis in insects is basically controlled by two hormones, ecdysone and juvenile hormone (JH). Ecdysone is an ecdysteroid that acts on the moulting of the larval instars. It is produced by the larval prothoracic glands in response to the prothoracicotrophic hormone (PTTH). Ecdysone is converted to its active form, 20-hydroxyecdysone (20-HE), in the fat body. In the adult stage the prothoracic glands disappear and ecdysone synthesis is overtaken by either ovarian cells, as in *A. aegypti,* (Hagedorn et al., 1975) or other abdominal cells, as in *D. melanogaster* (Bownes, 1982, 1989).

The JH is a sesquiterpenoid produced by a pair of organs at the base of the brain, called *corpora allata.* This hormone confers the juvenile character of the moults that occur in the immature instars. Its absence from the last larval instar has as consequence the moult to the adult stage. In the adult, JH may regulate vitellogenesis.

There is evidence that both JH and ecdysone act through the formation of a hormone/

receptor complex that enters the nucleus and binds to the DNA near the target genes (Wyatt et al., 1984a). It has been claimed that the insect JH receptor belongs to a homologous superfamily of nuclear hormone receptors that include those for steroids and thyroid hormones (Wyatt, 1990).

Several proteins and genes involved in insect sexual determination and others related to reproduction are the subject of a recent review (Wyatt, 1991). In contrast to the vertebrates, in insects the hormonal differences between sexes are not the only requisite for the occurrence of the vitellogenesis process. Factors intrinsic to the fat body are also needed for the differential programming in males and females. These factors, determined early in development, are partially expressed in the last immature instar and totally manifested in the adult stage (or after a moult in the absence of JH). Consequently, treatment with exogenous JH analogs induces a low level of Vg expression in immature insects of both sexes, with exception of the last larval instar, where females exhibit higher response than males. In the adult stage, the males in general do not synthesize Vg in response to the hormonal induction, while in females the expression is maximal (*B. germanica,* Kunkel, 1979; *L. migratoria,* Dhadialla & Wyatt, 1983; Chinzei & Wyatt, 1985; *B. mori,* Mine et al., 1983). Wyatt and coworkers (1984a) attributed sexual differences in Vg expression during *Locusta* development to changes in the chromatin structure. Furthermore, as discussed above, recent data indicate a direct involvement of a product of the *D. melanogaster* sex determination gene dsx in the sex-specific expression of the *yp* genes (Burtis et al., 1991).

Despite these observations, Vg is induced by JH in males of the cockroach *D. punctata* (Mundall et al., 1983). These males can even produce oocytes containing Vn after ovary implantation (Mundall et al., 1979; Stay et al., 1980). Additionally, residual Vg levels have been detected in normal males from different species (Kelly & Telfer, 1977; Chalaye, 1979; Lamy, 1979). In *R. prolixus* males the characteristic residual Vg haemolymph levels (Chalaye, 1979) can be rised either upon JH application (Chalaye & Lauverjat, 1985) or by feeding the colony with human blood (Valle et al., 1987).

In nematodes there is no evidence for hormonal activation of the *vit* genes. Vg synthesis in *C. elegans* is hermaphrodite-specific and sexual determination seems to be coordinately regulated in the intestine and in germinal tissues (Kimble & Sharrock, 1983). However, Spieth et al. (1988) found estrogen regulated expression of a *C. elegans* recombinant *vit* gene in transgenic lineages of this nematode.

Juvenile hormone stimulates vitellogenesis in the argasid tick *Ornithodoros parkeri* (Pound & Oliver, 1979). However, the gonadotrophic hormone in the Acarine order is supposed to be similar but not identical to the JH molecules active in insects (Connat et al., 1983).

In crustacea and in Thysanura insects the moult persists in the adults and moult and vitellogenesis cycles are correlated. In the isopods ecdysone is also required for Vg synthesis and secretion and for the oocyte growth (Suzuki, 1987). In the thysanurans it is believed that ecdysteroids induce previtellogenesis, while vitellogenesis seems to be controled by JH (Bitsch et al., 1985). Mating in this order also plays a role in the vitellogenesis induction (Rohdendorf & Watson, 1969).

The hormonal control of vitellogenesis has been studied in great detail in several orders of insects: Orthoptera, Hemiptera and Diptera. Examples from these insect orders as well as vertebrates will be analysed separately.

Orthoptera

In the orthoptera vitellogenesis is controlled by JH (Blattidae: *L. maderae,* Engelmann, 1969; *P. americana,* Bell, 1969; *B. germanica,* Kunkel, 1979; Acrididae: *L. migratoria,* Chen et al., 1976; Gryllidae; *A. domesticus,* Benford & Bradley, 1986). After JH treatment male and female fat bodies of *L. migratoria* exhibit both an increase in ploidy (Nair et al., 1981) and the development of structures characteristic of cells involved in intense protein synthesis (Lauverjat, 1977; Della-Cioppa & Engelmann, 1980). Most importantly, in female fat bodies JH specifically induces transcription of Vg mRNA at a high level. As a result, Vg mRNA can make up to 55% of the total poly (A +)-mRNA in this organ (Applebaum et al., 1981). In *L. migratoria* the Vg mRNA does not disappear concomitantly with the Vg synthesis decrease, suggesting its maintenance in the non-translated form (Chinzei et al., 1982). Vitellogenesis is more rapid after secondary hormonal stimulation (Chen et al., 1979;

Chinzei et al., 1982) and this has been correlated to a "memory effect", attributed to the persistence of receptors induced in the primary stimulation (Dhadialla et al., 1987).

It was recently demonstrated that different classes of *Locusta* proteins respond in different ways to JH: whereas Vg is induced *de novo* only in females, a 19 Kd polypeptide called persistent storage protein (PSP) is stimulated in both sexes and the apolipophorin III is not stimulated at all (Wyatt et al., 1992). The induction of *L. migratoria vit A* and *B* genes by the JH analog methoprene is coordinated (Dhadialla et al., 1987). Sequences flanking the 5' extremities are similar in both genes, indicating the presence of common regulatory signals (Wyatt et al., 1986). Nevertheless, assays to express locust Vg in *Drosophila* by P-element mediated transformation were not successful. Although recombinant locust Vg integration in the *Drosophila* genome has been obtained, translation did not occur, even in the presence of methoprene. The failure of *Drosophila* cells to recognize *Locusta* promoter signals is probably due to the evolutionary distance between both insects (Wyatt et al., 1986).

The *Locusta migratoria corpus allatum* is activated by brain neurosecretory cells (NSC) during oogenesis, probably through a humoral factor (McCaffery, 1976; Rembold et al., 1980). On the other hand, in the locust *S. gregaria* the *corpus allatum* stimulatory brain factor seems to act through the nervous pathway (Tobe et al., 1977).

It is believed that ecdysone is involved in the inhibition of JH induction of Vg synthesis (*L. migratoria,* Lagueux et al., 1977; *B. germanica,* Kunkel, 1979; *D. punctata,* Stay et al., 1980). In this order ovariectomy generally results in accumulation of Vg in the haemolymph (*P. americana,* Bell, 1969; *A. domesticus,* Bradley & Edwards, 1978; *L. maderae,* Engelmann, 1978; *N. cinerea,* Lanzrein et al., 1981; *L. migratoria,* Chinzei & Wyatt, 1985), although it has not been ascertained if this effect is due to removal of the ultimate "sink" of Vg accumulation rather than the source of ecdysone. This procedure has been successfully used for obtaining hemolymph Vg.

The adipokinetic hormone, secreted by the glandular lobe of the *corpus cardiacum,* is involved in lipid mobilization during locust flight (Applebaum, 1983). Recently it has been shown that in *L. migratoria* this hormone is also correlated with the negative control of vitellogenesis (Moshitzky & Applebaum, 1990). This is an interesting observation since in locusts the population migration starts in the previtellogenic phase and induces a reproductive diapause (Applebaum, 1983).

Hemiptera

In hemiptera, vitellogenesis is controlled by JH (*R. prolixus,* Coles, 1965; *Triatoma protracta,* Mundall & Engelmann, 1977; *Oncopeltus fasciatus,* Kelly & Telfer, 1977; *Dysdercus intermedius,* Dittmann et al., 1985). The hemiptera become competent to synthesize Vg in response to JH only after one moult in the absence of this hormone (Kelly & Hunt, 1982). Additionally, JH is necessary in the previtellogenic ovary in order to render the follicle cells able to react to a further exposure to the hormone (Davey, 1987).

The sexual dimorphism present in *R. prolixus* fat bodies is not prominent, as males of this species synthesize variable amounts of this protein (Chalaye, 1979; Valle et al., 1987). Nevertheless, JH application in males eliminates completely the remaining sexual dimorphism of fat body cells and also results in a dose-dependent occurrence of Vg in the hemolymph (Chalaye & Lauverjat, 1985). Although JH analogs are effective in *R. prolixus,* any of the molecular species known as JH could be identified in this hemipterin, suggesting that in this case JH function is exerted by some non-identified molecular species (Feder et al., 1988).

Allatectomy completely abolishes yolk deposition in the hematophagous *T. protracta* (Mundall & Engelmann, 1977) while in *R. prolixus* this procedure only slows down the vitellogenesis process, without eliminating it (Pratt & Davey, 1972a).

In the phytophagous hemipterin *D. intermedius* the *corpus allatum* of the virgin female is regulated by the brain (Dittmann et al., 1985). Accordingly, in the hematophagous *T. protracta* and *R. prolixus* the brain has an inhibitory effect on the *corpus allatum.* Nevertheless, in *R. prolixus* a transient neurosecretory brain stimulation of the *corpus allatum* has been also detected immediately after the meal (Mundall & Engelmann, 1977; Davey, 1987).

Mating in *T. protracta* activates the *corpus allatum* via the ventral nerve cord. Feeding in

this species serves as an additional stimulus for vitellogenesis (Mundall & Engelmann, 1977). On the other hand, mating in *R. prolixus* affects oviposition (Coles, 1965) but its action probably occurs through a myotropic factor released by the NSC (Davey, 1967). The oogenesis process is also increased in mated females and it is believed that the mating stimulus is mediated by a factor released by the female spermathecae (Davey, 1987). In the ovary terminal oocyte growth in each follicle is coordinated while the other oocytes stay in the previtellogenic phase. Virgin females, besides their tendency to retain vitellogenic eggs, accumulate oocytes in the previtellogenic phase, *i.e.*, below the "activation size" (Davey, 1967; Pratt & Davey, 1972b).

Juvenile hormone also acts directly on *R. prolixus* vitellogenic ovary increasing the condition known as "patency". This phenomenon, which consists of the enlarging of the interfollicular channels, is thought to occur through a Na+-K+-ATPase (Pratt & Davey, 1972a; Davey, 1981). This effect seems to be antagonized *in vivo* by antigonadotropins secreted by abdominal neurossecretory cells (Pratt & Davey, 1972b; Davey, 1981, 1987). It has been suggested that the function of these antigonadotropins is to assure a rapid cessation of vitellogenesis when the *corpus allatum* is inhibited by the brain (Davey, 1987).

Ecdysone inhibits the vitellogenesis and oviposition in *R. prolixus* and it was proposed that this hormone acts through the inhibition of JH production (Garcia et al., 1979). However, it was posteriorly verified that feeding in this species stimulates ecdysone synthesis, which increases until 4-5 days after feeding, shortly before the ovarian Vn peak (Feder et al., 1988).

Although it is generally accepted that *R. prolixus* oogenesis is controlled by hormones released in response to the abdominal stretching (Davey, 1987), Garcia & Azambuja (1985) suggested that induction of this process is dependent on a protein diet. In this work it was shown that feeding with non-proteic macromolecules induces abdominal stretching without stimulating oogenesis. It has also been observed that the blood feeding source has a profound influence over several physiological and biochemical aspects in *R. prolixus,* including molting, oviposition and Vg synthesis by the fat bodies (Lima Gomes et al., 1990; Valle et al., 1987, 1992a).

Lower Diptera (Orthorrapha)

Most part of the information from this group has been obtained from studies on mosquito vitellogenesis. The hormonal control of mosquito vitellogenesis generated a lot of controversy in the last two decades and has been the subject of several reviews (Fuchs & Kang, 1981; Borovsky, 1984; Kelly et al., 1987). The ovary is the site of ecdysone synthesis in *A. aegypti* (Hagedorn et al., 1975) and it was proposed that ecdysone is the hormone that triggers vitellogenesis in mosquitoes (Fallon et al., 1974). This proposal led to discussion because only pharmacological ecdysone quantities could induce Vg synthesis in previtellogenic females of the anautogenous mosquito, *A. aegypti* (Borovsky & Van Handel, 1979; Lea, 1982).

Further it was established that in the lower diptera JH regulates the previtellogenic phase while ecdysone controls the vitellogenic phase. The exposure of the fat bodies to JH in the previtellogenic phase reduces to physiological levels the amount of ecdysone necessary to promote Vg synthesis (Flanagan & Hagedorn, 1977; Kelly et al., 1981; Borovsky et al., 1985; Martinez & Hagedorn, 1987). This was confirmed by Ma et al. (1987, 1988). They measured Vg synthesis by *in vitro* cultured *A. aegypti* fat bodies using Vg-specific monoclonal antibodies in an enzyme-linked immunosorbent assay. They found that physiological quantities of 20-HE stimulated Vg synthesis and secretion in both blood-fed and non-blood-fed female fat bodies. However, fat bodies cultured immediately after eclosion did not respond to 20-HE. Prior treatment of these cultured fat bodies with JH permitted the development of competence to respond to 20-HE (Ma et al., 1988).

Raikhel & Lea (1990) have recently demonstrated that the previtellogenic role of JH, at least in part, is the stimulation of production of ribosomes in the fat body cells. Additionally, Dittmann et al (1989) have shown that JH also increases ploidy of the fat body cells.

Previtellogenic growth of the oocytes is also regulated by JH. The brain seems to regulate activity of the *corpus allatum* (Gwadz & Spielman, 1973; Hagedorn et al., 1979). The brain factor is suddenly released on the first day after adult emergence. Juvenile hormone is then secreted by the *corpus allatum* but, in

contrast to the brain factor, gradually during 2-3 days (Hagedorn et al., 1977). In *Culex pipiens* the oocyte growth is dependent on a head factor, released 4-8 minutes after the beginning of feeding (Baldridge & Feyereisen, 1986). However, in the autogenic mosquito *Aedes atropalpus* there is no brain control over the *corpus allatum* (Kelly et al., 1981).

The vitellogenic phase is initiated after feeding of non-autogenous species or after the adult emergence of autogenous species, when the so called *corpora cardiaca* stimulating factor (CCSF) is released from the ovary. This factor, not species-specific, stimulates secretion of the egg development neurosecretory hormone (EDNH) by the *corpus cardiacum* (Borovsky, 1982; Lea & Van Handel, 1982). In fact, EDNH is synthesized by the NSC and further transfered to the *corpus cardiacum,* where it is stored (Lea, 1967, 1972). The ovary is the target tissue for EDNH, where it induces ecdysone secretion. The action of EDNH is similar to the larval PTTH and the possibility of a structural similarity between these two hormones has been suggested (Hagedorn et al., 1979). Partial characterization of purified *A. aegypti* EDNH showed it is a polypeptide monomer of 19 Kd (Borovsky & Thomas, 1985). More recently a group of five peptides were purified from *A. aegypti* heads that elicit yolk deposition and secretion of ecdysteroids by ovaries of decapitated *A. atropalpus* (Matsumoto et al., 1989).

Ovarian ecdysone secretion seems to be mediated by cyclic AMP (Shapiro, 1983). In the lower diptera ecdysone induces the separation of follicles from the germaria in the ovary. This event is independent of additional brain factors (Beckemeyer & Lea, 1980). Changes in ecdysone titer also parallel changes in the Vg mRNA levels, with ecdysone increasing before and decreasing slowly, while Vg mRNA decays abruptly (Racioppi et al., 1986). These data corroborate the suggestion that ecdysone Vg synthesis induction acts at the transcriptional level (Kaczor & Hagedorn, 1980). Ecdysone increases Vg synthesis also in decapitated females, but high expression levels are achieved only after the blood meal. It was also verified that ecdysone and JH act directly in the fat body (Racioppi et al., 1986).

A. aegypti Vg mRNA transcription starts 1 h after blood feeding and reaches its maximum after 36 h (Racioppi et al., 1986). However Vg synthesis peaks at 27-30 hours after the blood meal and declines rapidly afterwards (Raikhel & Lea, 1983). At that time the lysosomal activity in the fat body cells is maximal and directed toward the specific degradation of Vg and organelles involved in its synthesis (Raikhel, 1986a, b).

The events involved in Vg synthesis termination are thought to depend on a decreasing titre of ecdysone. However, it is believed that Vg synthesis by the fat body is programmed to decline even if the exposure to ecdysone is prolonged (Bohm et al., 1978). A humoral factor released by mature ovaries that inhibits yolk deposition in less developed follicles has also been identified (Meola & Lea, 1972).

Oogenesis induction depends on absorption of peptides from the ingested blood (Chang & Judson, 1977a; Van Handel and Lea, 1984). Feeding itself or abdominal stretching do not seem to be involved, as previously believed (Larsen & Bodestein, 1959). In several mosquitoes an influence of the blood source on egg production was observed. In the majority of the tested species human blood results in the smallest egg production (Shelton, 1972; Nayar & Sauerman, 1977). This phenomenon was associated with a low content of isoleucine in the human blood (Chang & Judson, 1979). This amino acid does not interfere with the endocrine system and its effect is nutritional and direct, i.e., isolated fat bodies also respond to isoleucine (Chang & Judson, 1977b; Briegel, 1985).

Higher diptera (Cyclorrapha)

In this group of insects the Vgs, called yolk proteins (YP) are produced by both the fat body and the ovary in the majority of the species examined (Table II). Kambysellis (1977) identified three factors in the regulation of the vitellogenesis process in *D. melanogaster:* a brain factor, an ovarian factor that stimulates fat bodies YP synthesis (further recognized as ecdysone) and a thoracic factor (JH) involved in the YP uptake by ovaries.

Handler & Postlethwait (1977) verified that the brain factor is released upon adult eclosion and acts on the thoracic factor, necessary for Vg synthesis induction in the ovarian follicles. Subsequently it was shown that JH regulates the YP synthesis and uptake, while ecdysone is involved only in YP synthesis (Postlethwait & Handler, 1979).

Experiments using altered phenotype sex mutants of *D. melanogaster* suggested that sexual determination involves steps that promote ecdysteroid synthesis in females. These ecdysteroids would then activate synthesis of YP by fat bodies (Postlethwait et al., 1980). The authors have also shown that in isolated abdomens from male insects only ecdysone induces fat body YP synthesis and therefore proposed that ecdysone is the vitellogenic hormone acting in this organ while JH acts on the ovary. That JH is not able to induce YP synthesis in males was confirmed in other *Drosophila* species (Bownes, 1980).

Experiments with isolated abdomens also showed that female fat bodies can be induced by both hormones, whereas ovaries answer only to JH (Jowett & Postlethwait, 1980). These results provided additional evidence that ecdysone is the primary hormone responsible for YP synthesis induction in fat bodies. The fact that female fat bodies can be induced to produce YP by JH in isolated abdomens (Jowett & Postlethwait, 1980) was further explained by the finding that JH can induce an increase in ecdysteroid production (Schwartz et al., 1985).

There are two distinct lines of evidence concerning vitellogenesis control in *Drosophila*. At one side sexual hormonal differences, mainly ecdysteroids, are thought to be determinants of the process (Schwartz et al., 1985). On the other side, the sex determination genes rather than any sexually dimorphic hormone levels are said to cause the *yp* genes to be transcribed in females and repressed in males (Bownes, 1989). Recent data indicating the direct involvement of the sex determination gene dsx product in the expression of *yp* genes in Drosophila (Burtis et al., 1991) favors the second hypothesis. The control of the sex-determination genes over the *yp* genes in the fat body was shown to be direct and continuous. However, in the gonads these genes would be necessary for the follicle cell formation but would not control *yp* gene expression directly. Here the *yp* genes are regulated by specific factors deriving from the somatic tissue of the gonad (Bownes et al., 1990).

Another point of debate consists the site of ecdysteroid production in *Drosophila*. Different groups have detected ecdysteroid synthesis by ovarian cells but while some point the ovary as the major source of this hormone (Schwartz et al., 1985), others argue that ovarian ecdysteroids are transfered to the oocytes and that ovaries contribute only a small amount of the total hemolymph ecdysteroid content (Bownes, 1989).

In *M. domestica* juvenile hormone and ecdysone can induce Vg synthesis (Adams & Filipi, 1988). In this species both fat bodies and ovaries are stimulated by ecdysone and males are also responsive, but roughly 100 times less sensitive (Agui et al., 1991). Juvenile hormone has no effect on males whereas in females the ovaries are more intensively stimulated by this hormone than fat bodies (Agui et al., 1991).

The state of nutrition gradually affects oviposition. In females fed with a non-protein diet JH and ecdysone induce oogenesis redirecting resources so that YP expression in fat bodies is enhanced (Bownes & Blair, 1986). On the other hand Vg expression is induced by ecdysone but not by JH in males and females of *Sarcophaga bullata, Calliphora vicina, Phormia terrae-novae* and *Lucilia caesar* submitted to a non-protein diet (Huybrechts & De Loof, 1982).

Vg synthesis in *S. bullata* can be detected only in the fat body (Table II) and ecdysone has been identified as a major factor responsible for sexual differences in the activation of *vit* genes (Briers & Huybrechts, 1984). In this insect it was shown that the NSC participate in the activation of the endocrine glands involved in vitellogenesis (Cardoen et al., 1988).

Vertebrates

Vitellogenesis in vertebrates is under estrogen control. Hormonal treatment of vertebrate male adults can induce Vg synthesis (Tata & Smith, 1979) and studies on hormonal induction of Vg synthesis and cloning of *vit* genes in vertebrates are in general done by using hormonally treated males instead of females (Wahli et al., 1979; Protter et al., 1982). Despite the ease in inducing Vg synthesis in males, several nuclease hypersensitivity sites were detected in the *vit 2* gene of liver and oviduct cells of chicken embryos but not in other embryo tissues. Some of these sites are present before hormonal treatment, suggesting an embryonic targeting of these tissues for *vit* gene expression. Other sites are induced by 17-beta estradiol addition (Burch & Weintraub,

1983). It was further shown that estrogen induced hypersensitive sites are located in the vicinity of functional or imperfect estrogen response elements (ERE) corresponding sequences. It was suggested that these sites are adequate models to study chromatin restructuration events independent of transcription and that ERE would be only one component of a complex distal control region (Burch & Fischer, 1990). Binding of a palindromic sequence of the chicken *vit* gene promoter to the hormone/receptor complex and to other non-histone proteins not presenting tissue- or species-specificity was also detected (Feavers et al., 1987).

Estrogen treatment of vertebrates stimulates specifically synthesis of Vg and Vg mRNA (Baker & Shapiro, 1977; Jost et al., 1978; Martin et al., 1986). Estrogen also increases the half-life of Vg mRNA from 16 h to 3 weeks, thus reducing its cytoplasmic degradation (Brock & Shapiro, 1983). However, the involvement of vertebrate hepatocytes in Vg synthesis is not as conspicuous as that of insect fat body cells, where the amount of Vg mRNA may reach more than half of the poly(A +)-RNA (Applebaum et al., 1981).

Secondary hormonal induction is faster than the primary one. In addition, the control of *X. laevis vit A* and *vit B* gene expression is distinct after primary hormonal induction and coordinated after secondary induction (Wolffe & Tata, 1983). It was subsequently shown that mRNAs corresponding to *vit A1* and *vit B1* genes are more rapidly accumulated at levels 5 to 8 times higher than mRNAs coding for *vit A2* and *vit B2* (Ng et al., 1984).

X. laevis vit A expression is not associated with hypomethylation, indicating that changes in the methylation pattern are not a general prerequisite for gene activation (Gerber-Huber et al., 1983). On the other hand, a region with imperfect palindrome structure was detected in the third intron of the chicken *vit 2* gene. This region is flanked by a CpG dinucleotide that has demethylation kinetics similar to the kinetics of the Vg mRNA synthesis. This region is also able to bind a protein fraction from hepatocytes cytoplasmic extracts (Jost et al., 1987). Hypomethylation in the chicken vit gene extends to a repetitive element (*CR1*) located at the 3' end, in a region that exhibits changes in the chromatin structure. It was suggested that this element may play a role in the determination of the local chromatin conformational state (Van het Schip et al., 1987b).

Estrogen induced expression of *X. laevis* Vg A in human cancer cell cultures transfected with the *vit A2* genes indicated evolutionary conservation of factors and signals involved in the Vg control of expression (Klein-Hitpass et al., 1986).

CONCLUDING REMARKS

The great number of Vg post-translational modifications and the fact that it is a major protein in certain moments of the life cycle make Vg and the vitellogenesis process an extremely useful model for the study of the protein synthesis, maturation and secretion.

Despite being the major constituent of the eggs, its nutritional role during the embryonic development has been under discussion for an increasing number of species.

Comparison of the genes coding for Vg in different organisms has led to considerations about the evolutionary processes governing distinct species. Additionally, a number of gene sequences have been localized that confer expression specificity in relation to various parameters, like sex, tissue and hormones.

The number of molecular tools available to study Vg and the vitellogenesis process is increasing and investigations in these areas can contribute to the understanding of different mechanisms of regulation of gene expression and to the means by which these mechanisms are established during development.

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REFERENCES

ADAMS, T. S. & FILIPI, P. A., 1988. Interaction between juvenile hormone, 20-hydroxyecdysone, the corpus cardiacum-allatum complex, and the ovaries in regulating vitellogenin levels in the housefly, *Musca domestica*. *J. Insect Physiol., 34:* 11-19.

AGUI, N.; SHIMADA, T.; IZUMI, S. & TOMINO, S., 1991. Hormonal control of vitellogenin mRNA levels in the male and female housefly, *Musca domestica*. *J. Insect Physiol., 37:* 383-390.

APPLEBAUM, S. W., 1983. Regulation of locust vitellogenesis. *TIBS, 8:* 39-41.

APPLEBAUM, S. W.; JAMES, T. C.; WRESCHNER, D. H. & TATA, J. R., 1981. The preparation and characterization of locust vitellogenin messenger RNA and the synthesis of its complementary DNA. *Biochem. J., 193:* 209-216.

ATLAS, S. J.; ROTH, T. F. & FALCONE, A. J., 1978. Purification and partial characterization of *Culex pipiens fatigans* yolk protein. *Insect Biochem., 8:* 111-115.

BAERT, J.-L.; SAUTIERE, P. & PORCHET, M., 1984. Purification and characterization of oocyte vitellin from *Perinereis cultrifera* (polychaete annelid). *Eur. J. Biochem., 142:* 527-532.

BAERT, J.-L. & SLOMIANNY, M. C., 1987. Heterosynthetic origin of the major yolk protein, vitellin, in a nereid, *Perinereis cultrifera* (polychaete annelid). *Comp. Biochem. Physiol., 88B:* 1191-1199.

BAKER, B. S., 1989. Sex in flies: the splice of life. *Nature, 340:* 521-524.

BAKER, H. J. & SHAPIRO, D. J., 1977. Kinetics of estrogen induction of *Xenopus laevis* vitellogenin messenger RNA as measured by hybridization to complementary DNA. *J. Biol. Chem., 252:* 8428-8434.

BAKER, M. E., 1988. Is vitellogenin an ancestor of apolipoprotein B-100 of human low-density lipoprotein and human lipoprotein lipase? *Biochem. J., 255:* 1057-1060.

BALDRIDGE, G. D. & FEYEREISEN, R., 1986. Ecdysteroid titer and oocyte growth in the northern house mosquito, *Culex pipiens L. Comp. Biochem. Physiol., 83A:* 325-329.

BARNETT, T.; PACHL, C.; GERGEN, J. P. & WENSINK, P. C., 1980. The isolation and characterization of *Drosophila* yolk protein genes. *Cell, 21:* 729-738.

BAST, R. E. & TELFER, W. H., 1976. Follicle cell protein synthesis and its contribution to the yolk of cecropia moth oocyte. *Dev. Biol. 52:* 83-97.

BECKEMEYER, E. F. & LEA, A. O., 1980. Induction of follicle separation in the mosquito by physiological amounts of ecdysterone. *Science, 299:* 819-821.

BELL, W. J., 1969. Dual role of juvenile hormone in the control of yolk formation in *Periplaneta americana. J. Insect Physiol., 15:* 1279-1290.

BELOTE, J. M.; HANDLER, A. M.; WOLFNER, M. F.; LIVAK, K. J. & BAKER, B. S., 1985. Sex-specific regulation of yolk protein gene expression in *Drosophila. Cell, 40:* 339-348.

BENFORD, H. H. & BRADLEY, J. T., 1986. Early detection and juvenile hormone-dependence of cricket vitellogenin. *J. Insect Physiol., 32:* 109-116.

BITSCH, C.; BAHER, J. C. & BITSCH, J., 1985. Juvenile hormones in *Thermobia domestica* females: identification and quantification during biological cycles and after precocene application. *Experientia, 41:* 409-410.

BLUMENTHAL, T.; SQUIRE, M.; KIRTLAND, S.; CANE, J.; DONEGAN, M.; SPIETH, J. & SHARROCK, W., 1984. Cloning of a yolk protein gene family from *Caenorhabditis elegans. J. Mol. Biol., 174:* 1-18.

BOCTOR, F. N. & KAMEL, M. Y., 1976. Purification and characterization of two lipovitellins from eggs of the tick, *Dermacentor andersoni. Insect Biochem., 6:* 233-240.

BOHM, M. K.; BEHAN, M. & HAGEDORN, H. H., 1978. Termination of vitellogenin synthesis by mosquito fat body, a programmed response to ecdysterone. *Phys. Entomol., 3:* 17-25.

BOROVSKY, D., 1982. Release of egg development neurosecretory hormone in *Aedes aegypti* and *Aedes taeniorhynchus* induced by an ovarian factor. *J. Insect Physiol., 28:* 311-316.

BOROVSKY, D., 1984. Control mechanisms for vitellogenin synthesis in mosquitoes. *BioEssays, 1:* 264-267.

BOROVSKY, D. & THOMAS, B. R., 1985. Purification and partial characterization of mosquito egg development neurosecretory hormone: evidence for gonadotropic and steroidogenic effects. *Arch. Insect Biochem. Physiol., 2:* 265-281.

BOROVSKY, D.; THOMAS, B. R.; CARLSON, D. A.; WHISENTON, L. R. & FUCHS, M. S., 1985. Juvenile hormone and 20-hydroxyecdysone as primary and secondary stimuli of vitellogenesis in *Aedes aegypti. Arch. Insect Biochem. Physiol., 2:* 75-90.

BOROVSKY, D. & VAN HANDEL, E., 1979. Does ovarian ecdysone stimulate mosquitoes to synthesize vitellogenin? *J. Insect Physiol., 25:* 861-865.

BOROVSKY, D. & WHITNEY, P. L., 1987. Biosynthesis, purification, and characterization of *Aedes aegypti* vitellin and vitellogenin. *Arch. Insect Biochem. Physiol., 4:* 81-99.

BOSE, S. G. & RAIKHEL, A. S., 1988. Mosquito vitellogenin subunits originate from a common precursor. *Biochem. Biophys. Res. Comm., 155:* 436-442.

BOWNES, M., 1980. The use of yolk protein variations in *Drosophila* species to analyse the control of vitellogenesis. *Differ., 16:* 109-116.

BOWNES, M., 1982. Hormonal and genetic regulation of vitellogenesis in *Drosophila. Quart. Rev. Biol., 57:* 247-274.

BOWNES, M., 1989. The roles of juvenile hormone, ecdysone and the ovary in the control of *Drosophila* vitellogenesis. *J. Insect Physiol., 35:* 409-413.

BOWNES, M. & BLAIR, M., 1986. The effects of a sugar diet and hormones on the expression of the *Drosophila* yolk-protein genes. *J. Insect Physiol., 32:* 493-501.

BOWNES, M.; SHIRRAS, A.; BLAIR, M.; COLLINS, J. & COULSON, A., 1988. Evidence that insect embryogenesis is regulated by ecdysteroids released from yolk proteins. *Proc. Natl. Acad. Sci. USA, 85:* 1554-1557.

BOWNES, M.; STEINMANN-ZWICKY, M. & NOTHIGER, R., 1990. Differential control of yolk protein gene expression in fat bodies and gonads by the sex-determining gene *tra-2* of *Drosophila. EMBO J., 9:* 3975-3980.

BRADFIELD, J. Y. & WYATT, G. R., 1983. X-linkage of a vitellogenin gene in *Locusta migratoria. Chromosoma, 88:* 190-193.

BRADLEY, J. T. & EDWARDS, J. S., 1978. Yolk pro-

teins in the house cricket, *Acheta domesticus:* identification, characterization, and effect of ovariectomy upon their synthesis. *J. Exp. Zool., 204:* 239-248.

BRADLEY, J. T.; KERLE, K. K. & WOLFFE, K. G., 1987. Vitellogenin in the camel cricket *Ceutophilus* sp. (Orthoptera, Gryllacrididae). *J. Exp. Zool., 244:* 253-261.

BRENNAN, M. D.; WARREN, T. G. & MAHOWALD, A. P., 1980. Signal peptides and signal peptidase in *Drosophila melanogaster. J. Cell Biol., 87:* 516-520.

BRIEGEL, H., 1985. Mosquito reproduction: incomplete utilization of the blood meal protein for oogenesis. *J. Insect Physiol., 31:* 15-21.

BRIERS, T. & HUYBRECHTS, R., 1984. Control of vitellogenin synthesis by ecdysteroids in *Sarcophaga bullata. Insect Biochem., 14:* 121-126.

BROCK, M. L. & SHAPIRO, D. J., 1983. Estrogen stabilizes vitellogenin mRNA against cytoplasmic degradation. *Cell, 34:* 207-214.

BROOKES, V. J., 1986. The polypeptide structure of vitellogenin and vitellin from the cockroach, *Leucophaea maderae. Arch. Insect Biochem Physiol., 3:* 577-591.

BURCH, J. B. E. & FISCHER, A. H., 1990. Chromatin studies reveal that an ERE is located far upstream of a vitellogenin gene and that a distal tissue-specific hypersensitive site is conserved for two coordinatelly regulated vitellogenin genes. *Nuc. Ac. Res., 18:* 4157-4165.

BURCH, J. B. E. & WEINTRAUB, H., 1983. Temporal order of chromatin structural changes associated with activation of the major chicken vitellogenin gene. *Cell, 33:* 65-76.

BURTIS, K. C.; COSCHIGANO, K. T.; BAKER, B. S. & WENSINK, P. C., 1991. The doublesex proteins of *Drosophila melanogaster* bind directly to a sex-specific yolk protein gene enhancer. *EMBO J., 10:* 2577-2582.

BYRNE, B. M.; GRUBER, M. & AB, G., 1989. The evolution of egg yolk proteins. *Prog. Biophys. Molec. Biol., 53:* 33-69.

CARDOEN, J.; VAN COILLIE, C.; GEYSEN, J. & DE LOOF, A., 1988. Yolk polypeptide synthesis in the fat body of *Sarcophaga bullata:* localization, hormonal induction and cell-free translation. *Insect Biochem., 18:* 287-294.

CHALAYE, D., 1979. Étude immunochimique des protéines hémolymphatiques et ovocytaires de *Rhodnius prolixus* (Stal.). *Can. J. Zool., 57:* 329-336.

CHALAYE, D. & LAUVERJAT, S., 1985. Stimulation de la synthèse de vitellogenine chez le mâle de *Rhodnius prolixus* (Stal.) par un mimétique de l'hormone juvénile. *Can. J. Zool., 63:* 790-798.

CHALAYE, D.; QUEIROZ HADJ-IDRIS, A. E. & LAUVERJAT, S., 1983. Le tissu adipeux de *Rhodnius prolixus* (Stal.). Étude histochimique et ultrastructurale chez les larves du 5^{e} stade et chez les imagos. *Can. J. Zool., 61:* 1023-1031.

CHANG, H.-H. & BRADLEY, J. T., 1983. Vitellogenin synthesis and secretion in ovariectomized crickets. *Comp. Biochem. Physiol., 75B:* 733-737.

CHANG, Y.-Y. H. & JUDSON, C. L., 1977a. Peptides as stimulators of egg development neurosecretory hormone release in the mosquito *Aedes aegypti. Comp. Biochem. Physiol., 57C:* 147-151.

CHANG, Y.-Y. H. & JUDSON, C. L., 1977b. The role of isoleucine in differential egg production by the mosquito *Aedes aegypti* Linnaeus (Diptera: Culicidae) following feeding on human or guinea pig blood. *Comp. Biochem. Physiol., 57A:* 23-28.

CHANG, Y.-Y. H. & JUDSON, C. L., 1979. Amino acid composition of human and guinea pig blood proteins, and ovarian proteins of the yellow fever mosquito *Aedes aegypti;* and their effects on the mosquito egg production. *Comp. Biochem. Physiol., 62A:* 753-755.

CHEN, A. C.; KIM, H. R.; MAYER, R. T. & NORMAN, J. O., 1987. Vitellogenesis in the stable fly, *Stomoxys calcitrans. Comp. Biochem. Physiol., 88B:* 897-903.

CHEN, T. T., 1980. Vitellogenin in locustus (*Locusta migratoria*): translation of vitellogenin mRNA in *Xenopus* oocytes and analysis of the polypeptide products. *Arch. Biochem. Biophys., 201:* 266-276.

CHEN, T. T.; COUBLE, P.; ABU-HAKIMA, R. & WYATT, G. R., 1979. Juvenile hormone-controlled vitellogenin synthesis in *Locusta migratoria* fat body. Hormonal induction *in vivo. Dev. Biol., 69:* 59-72.

CHEN, T. T.; COUBLE, P.; DE LUCCA, F. L. & WYATT, G. R., 1976. Juvenile hormone control of vitellogenin synthesis in *Locusta migratoria.* In *The Juvenile Hormones.* (Ed. by Gilbert, L. I.), p. 505-529. Plenum Press, New York.

CHEN, T. T.; STRAHLENDORF, P. W. & WYATT, G. R., 1978. Vitellin and vitellogenin from locusts (*Locusta migratoria*). Properties and post-translational modification in the fat body. *J. Biol. Chem., 253:* 5325-5331.

CHINO, H.; YAMAGATA, M. & TAKAHASHI, K., 1976. Isolation and characterization of insect vitellogenin. Its identity with hemolymph lipoprotein II. *Biochim. Biophys. Acta., 44:* 349-353.

CHINZEI, Y.; CHINO, H. & TAKAHASHI, K., 1983. Purification and properties of vitellogenin and vitellin from a tick, *Ornithodoros moubata. J. Comp. Physiol., 152:* 13-21.

CHINZEI, Y.; WHITE, B. N. & WYATT, G. R., 1982. Vitellogenin mRNA in locust fat body: identification, isolation, and quantitative changes induced by juvenile hormone. *Can. J. Biochem., 60:* 243-251.

CHINZEI, Y. & WYATT, G. R., 1985. Vitellogenin titre in haemolymph of *Locusta migratoria* in normal adults, after ovariectomy, and in response to methoprene. *J. Insect Physiol., 31:* 441-445.

CHINZEI, Y. & YANO, I., 1985. Fat body is the site of vitellogenin synthesis in the soft tick, *Ornithodoros moubata. J. Comp. Physiol. B, 155:* 671-678.

CHO, W.-L.; DEITSCH, K. W. & RAIKHEL, A. S., 1991. An extraovarian protein accumulated in mosquito oocytes is a carboxypeptidase activated in embryos. *Proc. Natl. Acad. Sci. USA., 88:* 10821-10824.

COLES, G. C., 1965. Haemolymph proteins and yolk formation in *Rhodnius prolixus* Stal. *J. Exp. Biol., 43:* 425-431.

CONNAT, J.-L.; DUCOMMUN, J. & DIEHL, P.-A.,

1983. Juvenile hormone-like substances can induce vitellogenesis in the tick *Ornithodoros moubata* (Acarina: Argasidae). *Int. J. Invert. Reprod., 6:* 285-294.

COUBLE, P.; CHEN, T. T. & WYATT, G. R., 1979. Juvenile hormone-controlled vitellogenin synthesis in *Locusta migratoria* fat body: cytological development. *J. Insect Physiol., 25:* 327-337.

DAVEY, K. G., 1967. Some consequences of copulation in *Rhodnius prolixus. J. Insect Physiol., 13:* 1629-1636.

DAVEY, K. G., 1981. Hormonal control of vitellogenin uptake in *Rhodnius prolixus* Stal. *Amer. Zool., 21:* 701-705.

DAVEY, K. G., 1987. Inputs to the hormonal control of egg development in *Rhodnius prolixus. Mem. Inst. Oswaldo Cruz, 82 (Suppl. III):* 103-108.

DE BIANCHI, A. G., 1987. Biochemical aspects of *Musca domestica* vitellogenesis. *Mem. Inst. Oswaldo Cruz, 82 (Suppl. III):* 79-81.

DE BIANCHI, A. G.; COUTINHO, M.; PEREIRA, S. D.; MARINOTTI, O. & TARGA, H. J., 1985. Vitellogenin and vitellin of *Musca domestica*. Quantification and synthesis by fat bodies and ovaries. *Insect Biochem., 15:* 77-84.

DE BIANCHI, A. G.; WINTER, C. E. & TERRA, W. R., 1982. Vitellogenins and other haemolymph proteins involved in the oogenesis of *Rhyncosciara americana. Insect Biochem., 12:* 177-184.

DEJMAL, R. K. & BROOKES, V. J., 1972. Insect lipovitellin. Chemical and physical characteristics of a yolk protein from the ovaries of *Leucophaea maderae. J. Biol. Chem., 247:* 869-874.

DELLA-CIOPPA, G. & ENGELMANN, F., 1980. Juvenile hormone-stimulated proliferation of endoplasmic reticulum in fat body cells of a vitellogenic insect, *Leucophaea maderae* (Blattaria). *Biochem. Biophys. Res. Comm., 93:* 825-832.

DELLA-CIOPPA, G. & ENGELMANN, F., 1987. The vitellogenin of *Leucophaea maderae.* Synthesis as a large phosphorylated precursor. *Insect Biochem., 17:* 401-415.

DHADIALLA, T. S.; COOK, K. E. & WYATT, G. R., 1987. Vitellogenin mRNA in locust fat body: coordinate induction of two genes by a juvenile hormone analog. *Dev. Biol., 123:* 108-114.

DHADIALLA, T. S.; HAYS, A. R. & RAIKHEL, A. S., 1992. Characterization of the solubilized mosquito vitellogenin receptor. *Insect Biochem. Molec. Biol.,* in press.

DHADIALLA, T. S. & RAIKHEL, A. S., 1990. Biosynthesis of mosquito vitellogenin. *J. Biol. Chem., 265:* 9924-9933.

DHADIALLA, T. S. & WYATT, G. R., 1983. Juvenile hormone-dependent vitellogenin synthesis in *Locusta migratoria* fat body: inducibility related to sex and stage. *Dev. Biol., 96:* 436-444.

DITTMANN, F.; KOGAN, P. H. & HAGEDORN, H. H., 1989. Ploidy levels and DNA synthesis in fat body cells of the adult mosquito, *Aedes aegypti:* the role of juvenile hormone. *Arch. Insect Biochem. Physiol., 12:* 133-143.

DITTMANN, F.; TRENCZEK, T. & KLEEMANN-STUMPF, I., 1985. Juvenile hormone-controlled vitellogenin cycles in *Dysdercus intermedius* (Heteroptera). *J. Insect Physiol., 31:* 729-739.

ENGELMANN, F., 1969. Female specific protein: biosynthesis controlled by corpus allatum in *Leucophaea maderae. Science, 165:* 407-409.

ENGELMANN, F., 1978. Synthesis of vitellogenin after long-term ovariectomy in a cockroach. *Insect Biochem., 8:* 149-154.

ENGELMANN, F. & FRIEDEL, T., 1974. Insect yolk protein precursor, a juvenile hormone induced phosphoprotein. *Life Sciences, 14:* 587-594.

FALLON, A. M.; HAGEDORN, H. H.; WYATT, G. R. & LAUFER, H., 1974. Activation of vitellogenin synthesis in the mosquito *Aedes aegypti* by ecdysone. *J. Insect Physiol., 20:* 1815-1823.

FEAVERS, I. M.; JIRICNY, J.; MONCHARMONT, B.; SALUZ, H. P. & JOST, J. P., 1987. Interaction of two nonhistone proteins with the estradiol response element of the avian vitellogenin gene modulates the binding of estradiol-receptor complex. *Proc. Natl. Acad. Sci. USA, 84:* 7453-7457.

FEDER, D.; VALLE, D.; REMBOLD, H. & GARCIA, E. S., 1988. Azadirachtin-induced sterilization in mature females of *Rhodnius prolixus. Z. Naturforsch, 43c:* 908-913.

FISCHER, A., 1979. A vitellin-like antigen. *Naturwissenschaften, 66:* 316-317.

FISCHER, A. & SCHMITZ, K., 1981. Preparation, properties, and composition of *Nereis* vitellin, the yolk protein of the Annelid, *Nereis virens. Diff., 19:* 103-108.

FLANAGAN, T. R. & HAGEDORN, H. H., 1977. Vitellogenin synthesis in the mosquito: the role of juvenile hormone in the development of responsiveness to ecdysone. *Phys. Ent., 2:* 173-178.

FOURNEY, R. M.; PRATT, G. F.; HARNISH, D. G.; WYATT, G. R. & WHITE, B. N., 1982. Structure and synthesis of vitellogenin and vitellin from *Calliphora erythrocephala. Insect Biochem., 12:* 311-321.

FUCHS, M. S. & KANG, S.-K., 1981. Ecdysone and mosquito vitellogenesis: a critical apraisal. *Insect Biochem., 11:* 627-633.

GARABEDIAN, M. J.; HUNG, M.-C. & WENSINK, P. C., 1985. Independent control elements that determine yolk protein gene expression in alternative *Drosophila* tissues. *Proc. Natl. Acad. Sci. USA, 82:* 1396-1400.

GARABEDIAN, M. J.; SHEPHERD, B. M. & WENSINK, P. C., 1986. A tissue-specific transcription enhancer from the *Drosophila* yolk protein 1 gene. *Cell, 45:* 859-867.

GARCIA, E. S. & AZAMBUJA, P., 1985. A protein diet initiates oogenesis in *Rhodnius prolixus. Braz. J. Med. Biol. Res., 18:* 195-199.

GARCIA, M. L. M.; MELLO, R. P. & GARCIA, E. S., 1979. Ecdysone, juvenile hormone and oogenesis in *Rhodnius prolixus. J. Insect Physiol., 25:* 695-700.

GELLISSEN, G.; WAJC, E.; COHEN, E.; EMMERICH, H.; APPLEBAUM, S. W. & FLOSSDORF, J., 1976. Purification and properties of oocyte vitellin from the migratory locust. *J. Comp. Physiol., 108:* 287-301.

GEMMILL, R. M.; HAMBLIN, M.; GLASER, R. L.; RACIOPPI, J. V.; MARX, J. L.; WHITE, B. N.; CALVO, J. M.; WOLFNER, M. F. & HAGEDORN, H. H., 1986. Isolation of mosquito vitellogenin genes and induction of expression by 20-hydroxyecdysone. *Insect Biochem., 16:* 761-774.

GERBER-HUBER, S.; MAY, F. E. B.; WESTLEY, B. R.; FELBER, B. K.; HOSBACH, H. A.; ANDRES, A.-C. & RYFFELL, G. U., 1983. In contrast to other *Xenopus* genes the estrogen-inducible vitellogenin genes are expressed when totally methylated. *Cell, 33:* 43-51.

GERBER-HUBER, S.; NARDELLI, D.; HAEFLIGER, J.-A.; COOPER, D. N.; GIVEL, F.; GERMOND, J.-E.; ENGEL, J.; GREEN, N. M. & WAHLI, W., 1987. Precursor-product relationship between vitellogenin and the yolk proteins as derived from the complete sequence of a *Xenopus* vitellogenin gene. *Nuc. Acids Res., 15:* 4737-4760.

GIORGI, F.; BRADLEY, J. T.; VIGNALLI, R. & MAZZINI, M., 1989. An autoradiographic analysis of vitellogenin synthesis and secretion in the fat body of the stick insect *Bacillus rossius. Tis. & Cell, 21:* 517-524.

GOTTLIEB, T. A. & WALLACE, R. A., 1982. Intracellular glycosilation of vitellogenin in the liver of estrogen-stimulated *Xenopus laevis. J. Biol. Chem., 257:* 95-103.

GWADZ, R. W. & SPIELMAN, A., 1973. Corpus allatum control of ovarian development in *Aedes aegypti. J. Insect Physiol., 19:* 1441-1448.

HAFER, J.; FISCHER, A. & FERENZ, H. J., 1992. Identification of the yolk receptor protein in oocytes of *Nereis virens* (Annelida, polychaeta) and comparison with the locust vitellogenin receptor. *J. Comp. Physiol. B, 162:* 148-152.

HAGEDORN, H. H. & JUDSON, C. L., 1972. Purification and site of synthesis of *Aedes aegypti* yolk proteins. *J. Exp. Zool., 182:* 367-378.

HAGEDORN, H. H. & KUNKEL, J. G., 1979. Vitellogenin and vitellin in insects. *Ann. Rev. Entomol., 24:* 475-505.

HAGEDORN, H. H.; O'CONNOR, J. D.; FUCHS, M. S.; SAGE, B.; SCHLAEGER, D. A. & BOHM, M. K., 1975. The ovary as a source of alpha-ecdysone in an adult mosquito. *Proc. Nat. Acad. Sci. USA, 72:* 3255-3259.

HAGEDORN, H. H.; SHAPIRO, J. P. & HANAOKA, K., 1979. Ovarian ecdysone secretion is controlled by a brain hormone in an adult mosquito. *Nature, 282:* 92-94.

HAGEDORN, H. H.; TURNER, S.; HAGEDORN, E. A.; PONTECORVO, D.; GREENBAUM, P.; PFEIFFER, D.; WHEELOCK, G. & FLANAGAN, T. R., 1977. Postemergence growth of the ovarian follicles of *Aedes aegypti. J. Insect Physiol., 23:* 203-206.

HAMBLIN, M. T.; MARX, J. L.; WOLFNER, M. F. & HAGEDORN, H. H., 1987. The vitellogenin gene family of *Aedes aegypti. Mem. Inst. Oswaldo Cruz, 82 (Suppl. III):* 109-114.

HANDLER, A. M. & POSTLETHWAIT, J. H., 1977. Endocrine control of vitellogenesis in *Drosophila melanogaster:* effects of the brain and corpus allatum. *J. Exp. Zool., 202:* 389-402.

HARRINGTON, F. E. & EASTON, D. P., 1982. A putative precursor to the major yolk protein of the sea urchin. *Dev. Biol., 94:* 505-508.

HATZOPOULOS, P. & KAMBYSELLIS, M. P., 1987. Isolation and structural analysis of *Drosophila grimshawi* vitellogenin genes. *Mol. Gen. Genet., 206:* 475-484.

HAYS, A. R. & RAIKHEL, A. S., 1990. A novel protein produced by the vitellogenic fat body and accumulated in mosquito oocytes. *Roux's Arch. Dev. Biol., 199:* 114-121.

HOVEMANN, B. & GALLER, R., 1982. Vitellogenin in *Drosophila melanogaster:* a comparison of the YPI and YPII genes and their transcription products. *Nuc. Ac. Res., 10:* 2261-2274.

HOVEMANN, B.; GALLER, R.; WALLDORF, U.; KUPPER, H. & BAUTZ, E. K. F., 1981. Vitellogenin in *Drosophila melanogaster:* sequence of the yolk protein I gene and its flanking regions. *Nuc. Ac. Res., 9:* 4721-4734.

HUNG, M.-C. & WENSINK, P. C., 1983. Sequence and structure conservation in yolk proteins and their genes. *J. Mol. Biol., 164:* 481-492.

HUYBRECHTS, R. & DE LOOF, A., 1982. Similarities in vitellogenin and control of vitellogenin synthesis within the genera *Sarcophaga, Calliphora, Phormia* and *Lucilia* (Diptera). *Comp. Biochem. Physiol., 72B:* 339-344.

INDRASITH, L. S.; KINDLE, H. & LANZREIN, B., 1990. Solubilization, identification and localization of vitellogenin-binding sites in follicles of the cockroach *Nauphoeta cinerea. Arch. Insect Biochem. Physiol., 15:* 213-228.

INDRASITH, L. S.; SASAKI, T. & YAMASHITA, O., 1988. A unique protease responsible for selective degradation of a yolk protein in *Bombyx mori.* Purification, characterization and cleavage profile. *J. Biol. Chem., 263:* 1045-1051.

IRIE, K. & YAMASHITA, O., 1980. Changes in vitellin and other yolk proteins during embryonic development in the silkworm, *Bombyx mori. J. Insect Physiol., 26:* 881-817.

IRIE, K. & YAMASHITA, O., 1983. Egg-specific protein in the silkworm, *Bombyx mori:* purification, properties, localization and titre changes during oogenesis and embryogenesis. *Insect Biochem., 13:* 71-80.

IZUMI, S. & TOMINO, S., 1983. Vitellogenin synthesis in the silkworm, *Bombyx mori:* separate mRNAs encode two subunits of vitellogenin. *Insect Biochem., 13:* 81-85.

IZUMI, S.; TOMINO, S. & CHINO, H., 1980. Purification and molecular properties of vitellin from the silkworm, *Bombyx mori. Insect Biochem., 10:* 199-208.

JOST, J.-P.; OHNO, T.; PANYIM, S. & SCHUERCH, A. R., 1978. Appearance of vitellogenin mRNA sequences and rate of vitellogenin synthesis in chicken liver following primary and secondary stimulation by 17 beta-estradiol. *Eur. J. Biochem., 84:* 355-361.

JOST, J.-P.; SALUZ, H.; JIRICNY, J. & MONCHARMONT, B., 1987. Estradiol-dependent trans-acting factor binds preferentially to a dyad-symmetry structure within the third intron of the avian vitellogenin gene. *J. Cell. Biochem., 35:* 69-82.

JOWETT, T. & POSTLETHWAIT, J. H., 1980. The regulation of yolk polypeptide synthesis in *Drosophila* ovaries and fat body by 20-hydroxyecdysone and a juvenile hormone analog. *Dev. Biol., 80:* 225-234.

KACZOR, W. J. & HAGEDORN, H. H., 1980. The effects of alpha-amanitin and cordycepin on vitellogenin synthesis by mosquito fat body. *J. Exp. Zool., 214:* 229-233.

KAGEYAMA, T. & TAKAHASHI, S. Y., 1990. Purification and characterization of a cysteine proteinase from silkworm eggs. *Eur. J. Biochem., 193:* 203-210.

KAMBYSELLIS, M. P., 1977. Genetic and hormonal regulation of vitellogenesis in *Drosophila. Amer. Zool., 17:* 535-549.

KAWOOYA, J. K.; OSIR, E. O. & LAW, J. L., 1986. Physical and chemical properties of microvitellogenin; a protein from the egg of the tobacco hornworm moth, *Manduca sexta. J. Biol. Chem., 261:* 10844-10849.

KELLY, T. J.; ADAMS, T. S.; SCHWARTZ, M. B.; BIRNBAUM, M. J.; RUBENSTEIN, E. C. & IMBERSKI, R. B., 1987. Juvenile hormone and ovarian maturation in the diptera: a review of recent results. *Insect Biochem., 17:* 1089-1093.

KELLY, T. J.; FUCHS, M. S. & KANG, S.-H., 1981. Induction of ovarian development in autogenous *Aedes atrapalpus* by juvenile hormone and 20-hydrodyecdysone. *Int. J. Inv. Rep., 3:* 101-112.

KELLY, T. J. & HUNT, L.-M., 1982. Endocrine influence upon the development of vitellogenic competency in *Oncopeltus fasciatus. J. Insect Physiol., 28:* 935-941.

KELLY, T. J. & TELFER, W. H., 1977. Antigenic and electrophoreic variants of vitellogenin in *Oncopeltus* blood and their control by juvenile hormone. *Dev. Biol. 61:* 58-69.

KIMBLE, J. & SHARROCK, W. J., 1983. Tissue-specific synthesis of yolk proteins in *Caenorhabditis elegans Dev. Biol., 96:* 189-196.

KLASS, M. R.; WOLF, N. & HIRSH, D., 1979. Further characterization of a temperature-sensitive transformation mutant in *Caenorhabditis elegans. Dev. Biol., 69:* 329-355.

KLEIN-HITPASS, L.; SCHORPP, M.; WAGNER, U. & RYFFEL, G. U., 1986. An estrogen-responsive element derived from the 5' flanking region of the *Xenopus* vitellogenin A2 gene functions in transfected human cells. *Cell, 46:* 1053-1061.

KOLLER, C. N.; DHADIALLA, T. S. & RAIKHEL, A. S., 1989. Selective endocytosis of vitellogenin by oocytes of the mosquito, *Aedes aegypti:* an *in vitro* study. *Insect. Biochem., 19:* 693-702.

KONIG, R. & LANZREIN, B., 1985. Binding of vitellogenin to specific receptors in oocyte membrane preparations of the ovoviviparous cockroach *Nauphoeta cinerea. Insect Biochem., 15:* 735-747.

KULAKOSKY, P. C. & TELFER, W. H., 1987. Selective endocytosis in vitro by ovarian follicles from *Hyalophora cecropia. Insect Biochem., 17:* 845-858.

KUNKEL, J. G., 1979. Stages of vitellogenic competence in the cockroach. *Am. Zool., 19:* 999 (Abstr.).

KUNKEL, J. G. & PAN, M. L., 1976. Selectivity of yolk protein uptake: comparison of vitellogenins of two insects. *J. Insect Physiol., 22:* 809-818.

LAGUEUX, M.; HIRN, M. & HOFFMANN, J. A., 1977. Ecdysone during ovarian development in *Locusta migratoria. J. Insect Physiol., 23:* 109-119.

LAMY, M., 1979. Vitellogenèse en milieu mâle chez les Lépidoptères. Aspects endocrinologique et protéique. *Année Biol., 18:* 335-371.

LANZREIN, B.; WILHELM, R. & BUSCHOR, J., 1981. On the regulation of the corpora allata activity in adult females of the ovoviviparous cockroach *Nauphoeta cinerea.* In *Juvenile Hormone Biochemistry.* (Ed. by Pratt, J. E. & Brookes, G. T.). pp. 147-160. Elsevier North-Holland Biomedical Press, Amsterdam.

LARSEN, J. R. & BODESTEIN, D., 1959. The humoral control of egg maturation in the mosquito. *J. Exp. Zool., 140:* 343-381.

LAUVERJAT, S., 1977. L'evolution post-imaginal du tissu adipeux femelle de *Locusta migratoria* et son controle endocrine. *Gen. Comp. Endocr., 33:* 13-34.

LEA, A. O., 1967. The medial neurosecretory cells and egg maturation in mosquitoes. *J. Insect Physiol., 13:* 419-429.

LEA, A. O., 1972. Regulation of egg maturation in the mosquito by the neurosecretory system. The role of the corpus cardiacum. *Gen Comp. End., Suppl. 3:* 602-608.

LEA, A. O., 1982. Artifactual stimulation of vitellogenesis in *Aedes aegypti* by 20-hydroxyecdysone. *J. Insect Physiol., 28:* 173-176.

LEA, A. O. & VAN HANDEL, E., 1982. A neurosecretory hormone-releasing factor from ovaries of mosquitoes fed blood. *J. Insect Physiol., 28:* 503-508.

LIMA GOMES, J. E. P.; AZAMBUJA, P. & GARCIA, E. S., 1990. Comparative studies on the growth and reproductive performances of *Rhodnius prolixus* reared on different blood sources. *Mem. Inst. Oswaldo Cruz, 85:* 299-304.

LOCKE, J.; WHITE, B. N. & WYATT, G. R., 1987. Cloning and 5' end nucleotide sequences of two juvenile hormone-inducible vitellogenin genes of the african migratory locust. *DNA, 6:* 331-342.

MA, M.; GONG, H.; ZHANG, J.-Z. & GWADZ, R., 1987. Response of cultured *Aedes aegypti* fat bodies to 20-hydroxyecdysone. *J. Insect Physiol., 33:* 89-93.

MA, M.; ZHANG, J.-Z.; GONG, H. & GWADZ, R., 1988. Permissive action of juvenile hormone on vitellogenin production by the mosquito, *Aedes aegypti. J. Insect Physiol., 34:* 593-596.

MARTIN, M. B.; RIEGEL, A. T. & SCHOENBERG, D. R., 1986. Differential induction of vitellogenin gene transcription and total transcriptional activity by estrogen in *Xenopus laevis* liver. *J. Biol. Chem., 261:* 2355-2361.

MARTINEZ, T. & HAGEDORN, H. H., 1987. Development of responsiveness to hormones after a blood meal in the mosquito *Aedes aegypti. Insect Biochem., 17:* 1095-1098.

MARTINEZ, E. & WAHLI, W., 1989. Cooperative binding of estrogen receptor to imperfect estrogen-responsive DNA elements correlates with their synergistic hormone-dependent enhancer activity. *EMBO J., 8:* 3781-3791.

MASETTI, M. & GIORGI, F., 1989. Vitellin degrada-

tion in developing embryos of the stick insect *Carausius morosus*. *J. Insect Physiol., 35:* 689-697.

MASUDA, H. & OLIVEIRA, P. L., 1985. Characterization of vitellin and vitellogenin from *Rhodnius prolixus*. Identification of phosphorylated compounds in the molecule. *Insect Biochem., 15:* 543-550.

MATSUMOTO, S.; BROWN, M. R.; SUZUKI, A. & LEA, A. O., 1989. Isolation and characterization of ovarian ecdysteroidogenic hormones from the mosquito *Aedes aegypti*. *Insect Biochem., 19:* 651-656.

McCAFFERY, A. R., 1976. Effects of eletrocoagulation of cerebral neurosecretory cells and implantation of corpora allata on oocyte development in *Locusta migratoria*. *J. Insect Physiol., 22:* 1081-1092.

MEOLA, R. & LEA, A. O., 1972. Humoral inhibition of egg development in mosquitoes. *J. Med. Ent., 9:* 99-103.

MINE, E.; IZUMI, S.; KATSUKI, M. & TOMINO, S., 1983. Developmental and sex-dependent regulation of storage protein synthesis in the silkworm, *Bombyx mori*. *Dev. Biol., 97:* 329-337.

MOSHITZKY, P. & APPLEBAUM, S. W., 1990. The role of adipokinetic hormone in the control of vitellogenesis in locusts. *Insect Biochem., 20:* 319-323.

MUNDALL, E. & ENGELMANN, F., 1977. Endocrine control of vitellogenin synthesis and vitellogenesis in *Triatoma protracta*. *J. Insect Physiol., 23:* 825-836.

MUNDALL, E. C. & LAW, J. H., 1977. An investigation into the composition and structure of *Manduca sexta* vitellogenin. *Am. Zool., 17:* 863 (Abstr.).

MUNDALL, E. C. & LAW, J. H., 1979. Physical and chemical characterization of vitellogenin from the hemolymph and eggs of the tobacco hornworm, *Manduca sexta*. *Comp. Biochem. Physiol., 63B:* 459-468.

MUNDALL, E. C.; SZIBBO, C. M. & TOBE, S. S., 1983. Vitellogenin induced in adult male *Diploptera punctata* by juvenile hormone and juvenile hormone analogue: identification and quantitative aspects. *J. Insect Physiol., 29:* 201-207.

MUNDALL, E. C.; TOBE, S. S. & STAY, B., 1979. Induction of vitellogenin and growth of implanted oocytes in male cockroaches. *Nature, 282:* 97-98.

NAIR, K. K.; CHEN, T. T. & WYATT, G. R., 1981. Juvenile hormone-stimulated polyploidy in adult locust fat body. *Dev. Biol., 81:* 356-360.

NARDELLI, D.; GERBER-HUBER, S.; VAN HET SCHIP, F. D.; GRUBER, M.; AB, G. & WAHLI, W., 1987a. Vertebrate and nematode genes coding for yolk proteins are derived from a common ancestor. *Biochem., 26,* 6397-6402.

NARDELLI, D.; VAN HET SCHIP, F. D.; GERBER-HUBER, S.; HAEFLIGER, J.-A.; GRUBER, M.; AB, G. & WAHLI, W., 1987b. Comparison of the organization and fine structure of a chiken and a *Xenopus laevis* vitellogenin gene. *J. Biol. Chem., 262:* 15377-15385.

NAYAR, J. K. & SAUERMAN, D. M., 1977. The effects of nutrition on survival and fecundity in Florida mosquitoes. *J. Med. Ent., 14:* 167-174.

NG, S. S. & DAIN, J. A., 1976. The natural occurence of sialic acids. In *Biological Roles of Sialic Acid.* (Ed. by Rosenberg, A. & Schengrund, C.). pp. 59-102. Plenum Press, New York.

NG, W. C.; WOLFFE, A. P. & TATA, J. R., 1984. Unequal activation by estrogen of individual *Xenopus* vitellogenin genes during development. *Dev. Biol., 102:* 238-247.

NICOLARO, M.-L. & BRADLEY, J. T., 1980. Yolk proteins in developing follicles of the house cricket, *Acheta domesticus* (L.). *J. Exp. Zool., 212:* 225-232.

NORDIN, J. H.; GOCHOCO, C. H.; WOJCHOWSKI, D. M. & KUNKEL, J. G., 1984. A comparative study of the size-heterogeneous high mannose oligosaccharides of some insect vitellins. *Comp. Biochem. Physiol., 79B:* 379-390.

OLIVEIRA, P. L.; GONDIN, K. C.; GUEDES, D. M. & MASUDA, H., 1986. Uptake of yolk proteins in *Rhodnius prolixus*. *J. Insect Physiol., 32:* 859-866.

OLIVEIRA, P. L.; PETRETSKI, M. D. A. & MASUDA, H., 1989. Vitellin processing and degradation during embryogenesis in *Rhodnius prolixus*. *Insect Biochem., 19:* 489-498.

OPRESKO, L. K. & WILEY, H. S., 1987. Receptor-mediated endocytosis in *Xenopus* oocytes. *J. Biol. Chem., 262:* 4109-4115.

OSIR, E. O.; ANDERSON, D. R.; GRIMES, W. J. & LAW, J. H., 1986a. Studies on the carbohydrate moiety of vitellogenin from the tobacco hornworm, *Manduca sexta*. *Insect Biochem., 16:* 471-478.

OSIR, E. O. & LAW, J. H. (1986) Studies on uptake of vitellogenin from the tobacco hornworm, *Manduca sexta*. *Arch. Insect Biochem. Physiol., 3:* 513-528.

OSIR, E. O.; WELLS, M. A. & LAW, J. H., 1986b. Studies on vitellogenin from the tobacco hornworm, *Manduca sexta*. *Arch. Insect Biochem. Physiol., 3:* 217-233.

PAN, M. L.; BELL, W. J. & TELFER, W. H., 1969. Vitellogenic blood protein synthesis by insect fat body. *Science, 165:* 393-394.

PEFEROEN, M. & DE LOOF, A., 1986. Synthesis of vitellogenic and non-vitellogenic yolk proteins by the fat body and the ovary on *Leptinotarsa decemlineata*. *Comp. Biochem. Physiol., 83B:* 251-254.

PEFEROEN, M.; STYNEN, D. & DE LOOF, A., 1982. A re-examination of the protein pattern of the hemolymph of *Leptinotarsa decemlineata*, with special reference of vitellogenins and diapause proteins. *Comp. Biochem. Physiol., 72B:* 345-351.

PERASSI, R., 1973. Female specific proteins in *Triatoma infestans* haemolymph. *J. Insect Physiol., 19:* 663-671.

PEREIRA, S. D. & DE BIANCHI, A. G., 1983. Vitellogenin and vitellin of *Rhyncosciara americana:* further characterization and time of synthesis. *Insect Biochem., 13:* 323-332.

PICAUD, J.-L. & SOUTY, C., 1980. Démonstration par immunoautoradiographie de la synthèse de la vitellogénine par le tissu adipeux de *Porcellio dilatatus* Brandt (Crustacé, Isopode) *C. R. Acad. Sci. Paris, 290:* 1019-1021.

POSTLETHWAIT, J. H.; BOWNES, M. & JOWETT, T., 1980. Sexual phenotype and vitellogenin synthesis in *Drosophila melanogaster*. *Dev. Biol., 79:* 379-387.

POSTLETHWAIT, J. H. & GIORGI, F., 1985. Vitello-

genesis in insects. In *Developmental Biology, A Comprehensive Synthesis*. (Ed. by Browder, L. W.). pp. 85-136. Plenum Press, New York.

POSTLETHWAIT, J. H. & HANDLER, A. M., 1979. The roles of juvenile hormone and 20-hydroxyecdysone during vitellogenesis in isolated abdomens of *Drosophila melanogaster*. *J. Insect Physiol., 25:* 455-460.

POSTLETHWAIT, J. H. & KASCHNITZ, R., 1978. The synthesis of *Drosophila melanogaster* vitellogenin *in vivo,* in culture, and in a cell-free translation system. *FEBS Lett., 95:* 247-251.

POUND, J. M. & OLIVER, J. H., 1979. Juvenile hormone: evidence of its role in the reproduction of ticks. *Science, 206:* 355-357.

PRATT, G. E. & DAVEY, K. G., 1972a. The corpus allatum and oogenesis in *Rhodnius prolixus* (Stal.). I. The effects of allatectomy. *J. Exp. Biol., 56:* 201-214.

PRATT, G. E. & DAVEY, K. G., 1972b. The corpus allatum and oogenesis in Rhodnius prolixus (Stal.). III. The effect of mating. *J. Exp. Biol., 56:* 223-237.

PROTTER, A. A.; WANG, S.-Y.; SHELNESS, G. S.; OSTAPCHUK, P. & WILLIAMS, D. L., 1982. Isolation and characterization of a cDNA clone specific for avian vitellogenin II. *Nuc. Acids Res., 10:* 4935-4950.

RACIOPPI, J. V.; GEMMILL, R. M.; KOGAN, P. H.; CALVO, J. M. & HAGEDORN, H. H.; 1986. Expression and regulation of vitellogenin messenger RNA in the mosquito, *Aedes aegypti*. *Insect Biochem., 16:* 255-262.

RAIKHEL, A. S., 1984. The accumulative pathway of vitellogenin in the mosquito oocyte: a high-resolution immuno- and cytochemical study. *J. Ultrast. Res., 87:* 285-302.

RAIKHEL, A. S., 1986a. Lysosomes in the cessation of vitellogenin secretion by the mosquito fat body; selective degradation of Golgi complexes and secretory granules. *Tis. & Cell, 18:* 125-142.

RAIKHEL, A. S., 1986b. Role of lysosomes in regulating of vitellogenin secretion in the mosquito fat body. *J. Insect Physiol., 32:* 597-604.

RAIKHEL, A. S., 1987. The cell biology of mosquito vitellogenesis. *Mem. Inst. Oswaldo Cruz, 82 (Suppl. III):* 93-101.

RAIKHEL, A. S. & DHADIALLA, T. S., 1992. Accumulation of yolk proteins in insect oocytes. *Annu. Rev. Entomol., 37:* 217-251.

RAIKHEL, A. S.; DHADIALLA, T. S.; CHO, W.-L.; HAYS, A. R. & KOLLER, C. N., 1990. Biosynthesis and endocytosis of yolk proteins in the mosquito. In *Molecular Insect Science*. (Ed. by Hagedorn, H. H. et al.). pp. 147-154. Plenum Press, New York.

RAIKHEL, A. S. & LEA, A. O., 1983. Previtellogenic development and vitellogenin synthesis in the fat body of a mosquito: an ultrastructural and immunocytochemical study. *Tis & Cell, 15:* 281-300.

RAIKHEL, A. S. & LEA, A. O., 1986. Internalized proteins directed into accumulative compartments of mosquito oocytes by the specific ligand, vitellogenin. *Tis. & Cell, 18:* 559-574.

RAIKHEL, A. S. & LEA, A. O., 1987. Analysis of mosquito yolk protein by monoclonal antibodies. In *Molecular Entomology*. pp. 403-413. Alan R. Liss, Inc.

RAIKHEL, A. S. & LEA, A. O., 1990. Juvenile hormone controls previtellogenic proliferation of ribosomal RNA in the mosquito fat body. *Gen. Comp. Endocrinol., 77:* 423-434.

RAIKHEL, A. S.; PRATT, L. H. & LEA, A. O., 1986. Monoclonal antibodies as probes for processing of yolk protein in the mosquito; production and characterization. *J. Insect Physiol., 32:* 879-890.

REMBOLD, H.; EDER, J. & ULRICH, G. M., 1980. Inhibition of allatotropic activity and ovary development in *Locusta migratoria* by anti-brain-anti-bodies. *Z. Naturforsch, 35c:* 1117-1119.

RIDDELL, D. C.; HIGGINS, M. J.; MCMILLAN, B. J. & WHITE, B. N., 1981. Structural analysis of the three vitellogenin genes in *Drosophila melanogaster*. *Nuc. Ac. Res., 9:* 1323-1338.

RINTERKNECHT, E. & ROUSSEL, J.-P., 1978. Modifications ultrastructurales induites par les hormones juvéniles dans les cellules du corps gras de *Locusta migratoria L. Bull. Soc. Zool. France, 103:* 359-366.

ROHDENDORF, E. B. & WATSON, J. A. L., 1969. The control of reproductive cycles in the female firebrat, *Lepismodes inquilinus*. *J. Insect Physiol., 13:* 2085-2101.

ROHRHASTEN, A. & FERENZ, H.-J., 1986a. Properties of the vitellogenin receptor of isolated locust oocyte membranes. *Int. J. Invertebr. Reprod. Dev. 10:* 133-142.

ROHRKASTEN, A. & FERENZ, H.-J., 1986b. Solubilization of the locust *Locusta migratoria* vitellogenin receptor. *Biochim. Biophys. Acta., 860:* 577-582.

ROHRKASTEN, A.; FERENZ, H.-J.; BUSCHMANN-GEBHARDT, B. & HAFER, J., 1989. Isolation of the vitellogenin-binding protein from locust ovaries. *Arch. Insect Biochem. Physiol., 10:* 141-150.

ROTH, T. F. & PORTER, K. R., 1964. Yolk protein uptake in the oocyte of the mosquito *Aedes aegypti*. *L. J. Cell Biol., 20:* 313-332.

ROUSSET, A.; BITSCH, C. & BITSCH, J., 1987. Vitellogenins in the firebrat, *Thermobia domestica* (Packard): immunological quantification during reproductive cycles and in relation to insemination (Thysanura: Lepismatidae) *J. Insect Physiol., 33:* 593-601.

SAKAI, N.; MORI, S.; IZUMI, S.; HAINO-FUKUSHIMA, K.; OGURA, T.; MAEKAWA, H. & TOMINO, S., 1988. Structures and expression of mRNAs coding for major plasma proteins of *Bombyx mori*. *Biochim. Biophys. Acta., 949:* 224-232.

SALISBURRY, N.; CALAPRICE, N. & TRIPLETT, E. L., 1980. Amphibian embryo protease inhibitors. VI. Maternal origin and identity with lipovitellin heavy subunit. *Cell Diff., 9:* 219-227.

SCHWARTZ, M. B.; KELLY, T. J.; IMBERSKI, R. B. & RUBENSTEIN, E. C., 1985. The effects of nutrition and methoprene treatment on ovarian ecdysteroid synthesis in *Drosophila melanogaster*. *J. Insect Physiol., 31:* 947-957.

SHAPIRO, J. P., 1983. Ovarian cyclic AMP and response to a brain hormone from the mosquito *Aedes aegypti*. *Insect Biochem., 13:* 273-279.

SHARROCK, W. J., 1983. Yolk proteins of *Caenorhabditis elegans*. *Dev. Biol., 96:* 182-188.

SHARROCK, W. J., 1984. Cleavage of two yolk pro-

teins from a precursor in *Caenorhabditis elegans*. *J. Mol. Biol., 174:* 419-431.

SHELTON, R. M., 1972. The effects of blood source and quantity on production of eggs by *Culex salinarius* coquillett (Diptera: Culicidae). *Mosquito News, 32:* 31-37.

SHIRK, P. D.; BEAN, D.; MILLEMANN, A. M. & BROOKES, V. J., 1984. Identification, synthesis, and characterization of the yolk polypeptides of *Plodia interpunctella*. *J. Exp. Zool., 232:* 87-98.

SHYU, A.-B.; BLUMENTHAL, T. & RAFF, R. A., 1987. A single gene encoding vitellogenin in the sea urchin *Strongylocentrotus purpuratus:* sequence at the 5' end. *Nuc. Ac. Res., 15:* 10405-10417.

SHYU, A.-B.; RAFF, R. A. & BLUMENTHAL, T., 1986. Expression of the vitellogenin gene in female and male sea urchin. *Proc. Natl. Acad. Sc. USA, 83:* 3865-3869.

SILVA, R.; FISCHER, A. H. & BURCH, J. B. E., 1989. The major and minor chicken vitellogenin genes are each adjacent to partially deleted pseudogene copies of the other. *Mol. Cell. Biol., 9:* 3557-3562.

SOUTY, C., 1983. Démonstration d'une alternance des pics de synthèse des fractions, respectivement endogène, du vitellus protéique chez l'Oniscoide *Porcellio dilatatus Brandt. C. R. Acad. Sci. Paris, 296:* 221-223.

SPIETH, J. & BLUMENTHAL, T., 1985. The *Caenorhabditis elegans* vitellogenin gene family includes a gene encoding a distantly related protein. *Mol. Cell. Biol., 5:* 2495-2501.

SPIETH, J.; DENISON, K.; KIRTLAND, S.; CANE, J. & BLUMENTHAL, T., 1985a. The *C. elegans* vitellogenin genes: short sequence repeats in the promoter regions and homology to the vertebrate genes. *Nuc. Ac. Res., 13:* 5283-5295.

SPIETH, J.; DENISON, K.; ZUCKER, E. & BLUMENTHAL, T., 1985b. The nucleotide sequence of a nematode vitellogenin gene. *Nuc. Ac. Res., 13:* 7129-7138.

SPIETH, J.; MACMORRIS, M.; BROVERMAN, S.; GREENSPOON, S. & BLUMENTHAL, T., 1988. Regulated expression of a vitellogenin fusion gene in transgenic nematodes. *Dev. Biol., 130:* 285-293.

STAY, B.; FRIEDEL, T.; TOBE, S. S. & MUNDALL, E. C., 1980. Feedback control of juvenile hormone synthesis in cockroaches: possible role for ecdysterone. *Science, 207:* 898-900.

STEYRER, E.; BARBER, D. L. & SCHNEIDER, W. J., 1990. Evolution of lipoprotein receptors. The chicken oocyte receptor for very low density lipoprotein and vitellogenin binds the mammalian ligand apolipoprotein E. *J. Biol. Chem., 265:* 19575-19581.

STORELLA, J. R. & KUNKEL, J. G., 1979. Processing and utilization of vitellin in the cockroach egg. *Am. Zool., 19:* 999 (Abstr.).

STORELLA, J. R.; WOJCHOWSKI, D. M. & KUNKEL, J. G., 1985. Structure and embryonic degradation of two native vitellins in the cockroach, *Periplaneta americana*. *Insect Biochem., 15:* 259-275.

SUZUKI, S., 1987. Vitellins and vitellogenins of the terrestrial isopod, *Armadillidium vulgare*. *Biol. Bull., 173:* 345-354.

TAKAHASHI, S. Y., 1987. Post-translational processing, by phosphorylation, of vitellogenin and vitellin from the silkworm, *Bombyx mori*. *Comp. Biochem. Physiol., 87B:* 255-266.

TATA, J. R. & SMITH, D. F., 1979. Vitellogenesis: a versatile model for hormonal regulation of gene expression. *Recent Prog. Horm. Res., 35:* 47-95.

TERPSTRA, P. & AB, G., 1988. Homology of *Drosophila* yolk proteins and the triacylglycerol lipase family. *J. Mol. Biol., 202:* 663-665.

TOBE, S. S.; CHAPMAN, C. S. & PRATT, G. E., 1977. Decay in juvenile hormone biosynthesis by insect corpus allatum after nerve transection. *Nature, 268:* 728-730.

TREWITT, P. M.; HEILMANN, L. J.; DEGRUGILLIER, S. S. & KUMARAN, A. K., 1992. The boll weevil vitellogenin gene: nucleotide sequence, structure, and evolutionary relationship to nematode and vertebrate vitellogenin genes. *J. Mol. Evol., 34:* 478-492.

TSUCHIDA, K.; KAWOOYA, J. K.; LAW, J. H. & WELLS, M. A., 1991. Isolation and characterization of two follicle-specific proteins from eggs of *Manduca sexta*. *Insect Biochem. Molec. Biol., 22:* 89-98.

VALLE, D.; GARCIA, E. S. & GOLDENBERG, S., 1992a. Influence of the blood meal source on vitellogenin synthesis by isolated fat bodies of *Rhodnius prolixus*. *Insect Biochem., 22:* 159-166.

VALLE, D.; KUN, J.; LINSS, J.; GARCIA, E. S. & GOLDENBERG, S., 1992b. *Rhodnius prolixus* vitellogenin is synthesized as high molecular weight precursors. Isolation of a vitellogenin cDNA clone. *Insect Biochem Molec. Biol.,* in press.

VALLE, D.; LIMA GOMES, J. E. P.; GOLDENBERG, S. & GARCIA, E. S., 1987. *Rhodnius prolixus* vitellogenesis: dependence upon the blood source. *J. Insect Physiol., 33:* 249-254.

VAN HANDEL, E. & LEA, A. O., 1984. Vitellogenin synthesis in blood-fed *Aedes aegypti* in the absence of the head, thorax and ovaries. *J. Insect Physiol., 30:* 871-875.

VAN HET SCHIP, F. D.; SAMALLO, J.; BROOS, J.; OPHUIS, J.; MOJET, M.; GRUBER, M. & AB, G., 1987a. Nucleotide sequence of a chicken vitellogenin gene and derived amino acid sequence of the encoded yolk precursor protein. *J. Mol. Biol., 196:* 245-260.

VAN HET SCHIP, F.; SAMALLO, J.; MEIJLINK, F.; GRUBER, M. & AB, G., 1987b. A new repetitive element of the CR1 family downstream of the chicken vitellogenin gene. *Nuc. Ac. Res., 15:* 4193-4202.

WAHLI, W., 1988. Evolution and expression of vitellogenin genes. *TIG, 4:* 227-232.

WAHLI, W. & DAWID, I. B., 1980. Isolation of two closely related vitellogenin genes, including their flanking regions, from a *Xenopus laevis* gene library. *Proc. Natl. Acad. Sci. USA, 77:* 1437-1441.

WAHLI, W.; DAWID, I. B.; WYLER, T.; JAGGI, R. B.; WEBER, R. & RYFFELL, G. U., 1979. Vitellogenin in *Xenopus laevis* is encoded in a small family of genes. *Cell, 16:* 535-549.

WANG, X.-Y; COLE, K. D. & LAW, J. H., 1988. cDNA cloning and deduced amino acid sequence of microvitellogenin, a female specifc hemolymph and egg protein from the tobacco hornworm, *Manduca sexta*. *J. Biol. Chem., 263:* 8851-8855.

WARREN, T. G. & MAHOWALD, A. P., 1979. Isolation and partial chemical characterization of the three major yolk polypeptides from *Drosophila melanogaster*. *Dev. Biol., 68:* 130-139.

WOJCHOWSKI, D. M.; PARSONS, P.; NORDIN, J. H. & KUNKEL, J. G., 1986. Processing of provitellogenin in insect fat body: a role for high-mannose oligosaccharide. *Dev. Biol., 116:* 422-430.

WOLFFE, A. P. & TATA, J. R., 1983. Coordinate and non-coordinate estrogen-induced expression of A and B groups of vitellogenin genes in male and female *Xenopus* hepatocytes in culture. *Eur. J. Biochem., 130:* 365-372.

WYATT, G. R., 1988. Vitellogenin synthesis and the analysis of juvenile hormone action in locust fat body. *Can. J. Zool., 66:* 2600-2610.

WYATT, G. R., 1990. Developmental and juvenile hormone control of gene expression in locust fat body. In *Molecular Insect Science.* (Ed. by Hagedorn, H. H. et al.). pp. 163-172.

WYATT, G. R., 1991. Gene regulation in insect reproduction. *Invert. Reprod. Dev., 20:* 1-35.

WYATT, G. R.; DHADIALLA, T. S. & ROBERTS, P. E., 1984a. Vitellogenin synthesis in locust fat body: juvenile hormone-stimulated gene expression. In *Biosynthesis, Metabolism and Mode of Action of Invertebrate Hormones.* (Ed. by Hoffmann, J. & Porchet, M.). pp. 475-484. Springer-Verlag, Berlin Heidelberg.

WYATT, G. R.; KANOST, M. R.; CHIN, B. C.; COOK, K. E.; KAWASOE, B. M. & ZHANG, J., 1992. Juvenile hormone analog and injection effects on locust hemolymph protein synthesis. *Arch. Insect Biochem. Physiol., 20:* 167-180.

WYATT, G. R.; KANOST, M. R.; LOCKE, J. & WALKER, V. K., 1986. Juvenile hormone-regulated locust vitellogenin genes: lack of expression after transfer into *Drosophila*. *Arch. Insect Biochem. Physiol., Suppl. 1:* 35-46.

WYATT, G. R.; LOCKE, J. & BRADFIELD, J. Y., 1984b. The vitellogenin genes of *Locusta migratoria* and other insects. In *Advances in Invertebrate Reproduction.* vol. 3 (Ed. by Engels, W. et al.). Elsevier Science Publishers. B. V.

YAMASHITA, O. & IRIE, K., 1980. Larval hatching from vitellogenin-deficient eggs developed in male hosts of the silkworm. *Nature, 283:* 385-386.

YAN, Y. L.; KUNKERT, C. J. & POSTLETHWAIT, J. H., 1987. Sequence homologies among the three yolk polypeptide (yp) genes in *Drosophila melanogaster*. *Nuc. Ac. Res., 15:* 67-85.

ZHAI, Q.-H.; POSTLETHWAIT, J. H. & BODLEY, J. W., 1984. Vitellogenin synthesis in the lady beetle *Coccinella septempunctata*. *Insect Biochem., 14:* 299-305.

ZHANG, J.-Z. & WYATT, G. R., 1990. A new member of a low molecular weight hemolymph protein family from *Locusta migratoria*. In *Molecular and Insect Science.* (Ed. by Hagedorn, H. H.; Hildebrand, J. G.; Kidwell, M. G. & Law, J. H.). pp. 385. Plenum Press, New York.

ZHU, J.; INDRASITH, L. S. & YAMASHITA, O., 1986. Characterization of vitellin, egg-specific protein and 30 kDa protein from *Bombyx* eggs, and their fates during oogenesis and embryogenesis. *Biochem. Biophys. Acta, 882:* 427-436.

ZONGZA, V. & DIMITRIADIS, G. J., 1988. Vitellogenesis in the insect *Dacus oleae*. Isolation and characterization of yolk protein mRNA. *Insect Biochem., 18:* 651-660.

ZUCKER-APRISON, E. & BLUMENTHAL, T., 1989. Potential regulatory elements of nematode vitellogenin genes revealed by interspecies sequence comparison. *J. Mol. Evol., 28:* 487-496.