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THYMIC "NURSE" CELLS EXPRESS EXTRACELLULAR MATRIX PROTEINS

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Thymic "nurse" cells (TNC) are lymphoepithelial complexes located in the outer thymus cortex, that are formed by epithelial cells which may enclose 20 to 200 thymocytes of mainly immature phenotype (H. Wekerle et al., 1980, *J. Exp. Med., 151:* 925-944). TNC create special microenvironmental conditions to thymocyte differentiation and/or proliferation: they express MHC antigens (H. Wekerle & U. P. Ketelsen, 1980, *Nature, 283*: 402-404) and secrete thymic hormones, such as thymulin (M. Nakayama et al., 1984, Proceedings of the 6th European Immunology Meeting, Interlaken, p. 264). Lastly, TNC may be involved in thymocyte education by presenting self antigens to very immature thymocytes.

Considering the increasing evidence coming out from our laboratory that extracellular matrix (ECM) components may play a role in thymus physiology (J. Lannes-Vieira et al., 1991, *J.*

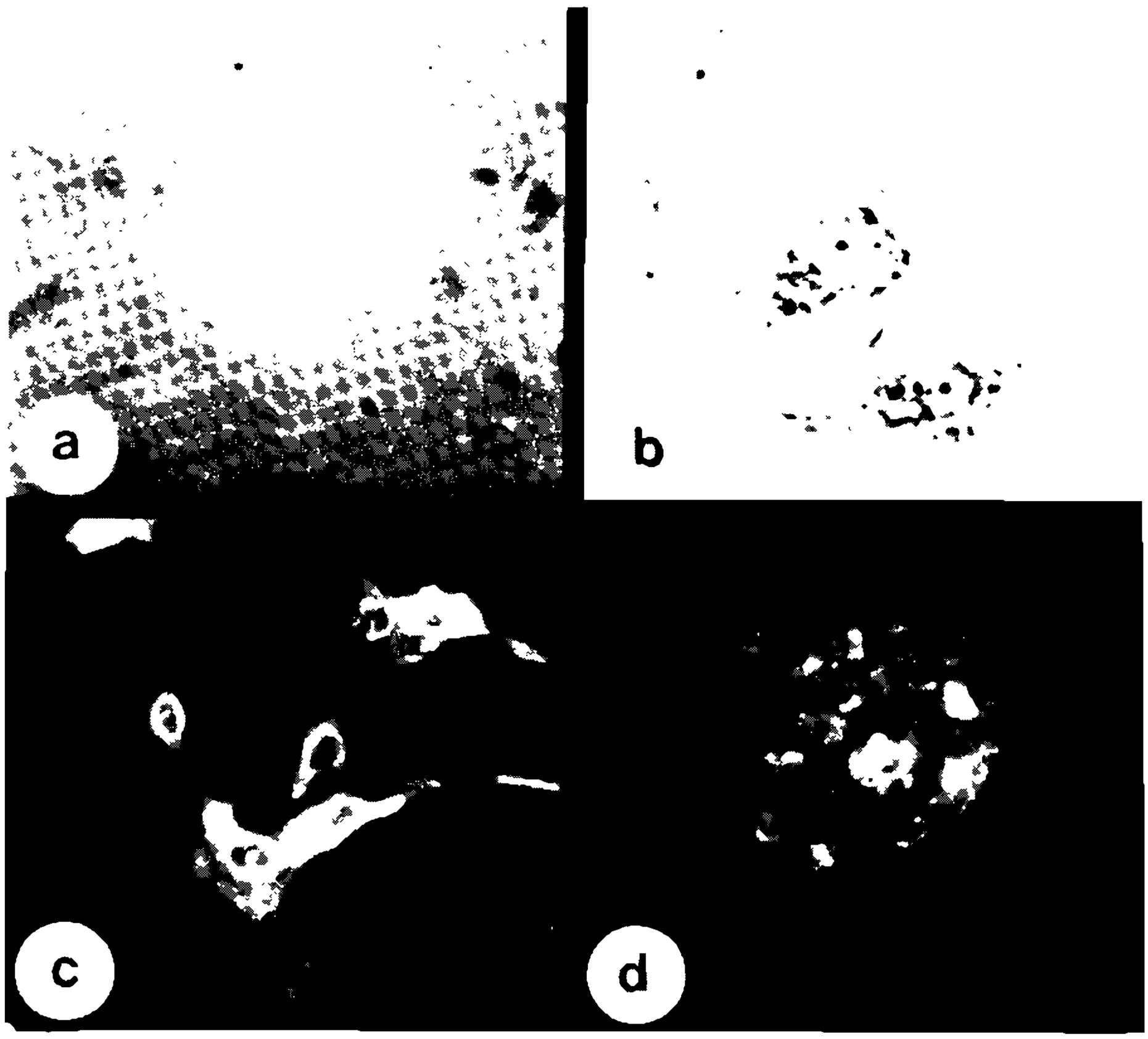

Fig. 1: thymic "nurse" cell complexes and their modulation by anti-fibronectin antibodies. a, b: light microscopy of freshly isolated TNC (a) or 24 cultured epithelial cells (b). X 960. c, d: fibronectin labeling of 72 h control (c) or anti-fibronectin treated (d) cultures. X 750.

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For this purpose, we cultured TNC isolated from C57BL/6 mice (M. P. Houben-Defresne et al., 1982, *Leukemia Res.*, *6*: 231-241) for 72 h in complete RPMI.

As expected, TNC adhered to culture plates and began to release thymocytes originating epithelial cultures, after 24 h of incubation (Fig. 1a, b). As shown by immunocytochemistry, these epithelial cultures expressed ECM proteins such as fibronectin, laminin and type IV collagen (Fig. 1c).

We then asked the question whether this ECM protein expression by TNC-derived epithelial cells would influence epithelial-lymphocyte interactions during thymocyte differentiation. For this purpose, distinct anti-ECM or control antibodies were added 24 h after cell plating. We observed that TNC cultured in the presence of anti-fibronectin or anti-type IV collagen antibodies presented a delay in thymocyte release as compared to controls, remaining as lymphoepithelial complexes for a longer time (Fig. 1d). When anti-laminin antibody was applied a weaker effect could be noted. Interestingly, incubation with anti-laminin antibody clearly increased ECM protein secretion by TNC-derived epithelial cells, suggesting a possible feedback effect.

The data reported herein suggest that TNC produce ECM components and that these molecules might play a role in epithelial-thymocyte interactions in TNC complexes, as shown by a modulation of thymocyte release with anti-ECM antibodies. Particularly regarding fibronectin, our findings are in keeping with the demonstration of fibronectin receptors in immature thymocytes (P. M. Cardarelli & M. D. Pierschbacher, 1986, *Proc. Natl Acad. Sci. USA*, *83*: 2647-2651).

Finally, our data indicate that TNC complexes might be regarded as a potentially useful model in the general study on the functions of ECM components in the thymus.