Abstract

Functional analysis of the thymic microenvironment using recombinant single chain antibodies

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Thymic stromal cells play a crucial role in T lymphocyte development, although the precise molecular interactions that are involved are largely unknown. To investigate these processes, we used a phage display library expressing recombinant single chain antibodies (scFv) [1] and have selected reagents with specificity for molecules expressed on the surface of cortical epithelial cells using either thymic stromal cells [2] or purified microenvironmental molecules as selection substrate. The majority of the scFv recognise evolutionarily conserved epitopes present in the thymus of a wide range of species including human, mouse, rat, pig and chicken. The molecules detected have been analysed by Western blotting; they include the gp200-MR6 antigen [3], previously identified only in the human thymus, while others are novel thymic molecules. Some of these scFv influence T cell development in

fetal thymic organ culture, indicating that their target molecules play an important role in the interaction between developing thymocytes and the epithelial microenvironment. Others have a direct differentiative effect on epithelium, suggesting that their ligand may play a role in thymocyte-epithelial crosstalk. Our data highlight the power of phage display technology for the selection of specific reagents, for detection of conserved epitopes/molecules on thymic epithelium and for the production of recombinant scFv whose small size enhances tissue penetration and therefore their efficacy in functional analysis.

References

- [1] A. Nissim, H.R. Hoogenboom, I.M. Tomlinson, G. Flynn, C. Midgley, D. Lane and G. Winter, *EMBO J.* **13** (1994), 692.
- [2] D.B. Palmer, A.J.T. George and M.A. Ritter, *Immunology* **91** (1997), 473.
- [3] P.F. McKay, N. Imami, M. Johns, D.A. Taylor-Fishwick, L.M. Sedibane, N.F. Totty, N.F. Hsuan, D.B. Palmer, A.J.T. George, B.M.J. Foxwell and M.A. Ritter, *Eur. J. Immunol.* **28** (1998), 4071.