Annotated Bibliography
1994-1997

1994

Tanaka T, Duke-Cohan JS, Kameoka J, Yaron A, Lee I, Schlossman SF, Morimoto C. Enhancement of antigen-induced T-cell proliferation by soluble CD26/dipeptidyl peptidase IV. *Proc Natl Acad Sci U S A* (1994) 91: 3082-6.

Evidence that there may be a soluble circulating molecule with catalytic properties similar to those of CD26, the canonical dipeptidyl peptidase IV (DPPIV) that has a modifying effect upon the functional activity of circulating lymphocytes. CD26 is a membrane antigen raising the question of whether the circulating activity was a proteolytic product, an alternative splice variant, or an unrelated gene product. The activity reacts with anti-CD26 monoclonal antibodies and levels may vary with immune status, implying a T cell origin. It is the subsequent purification of this activity to apparent homogeneity that leads to the identification of the secreted human attractin splice variant.

Lu D, Willard D, Patel IR, Kadwell S, Overton L, Kost T, Luther M, Chen W, Woychik RP, Wilkison WO, et al. Agouti protein is an antagonist of the melanocyte-stimulating-hormone receptor. Nature (1994) 371: 799-802.

Report that the agouti protein is a direct antagonist of a-MSH binding to the melanocortin receptors, thereby influencing pigmentation through the Mc1R and perhaps energy metabolism through the Mc4R. Is the antagonism direct or are there accessory molecules that aid in this process?

1995

Duke-Cohan JS, Morimoto C, Rocker JA, Schlossman SF. A novel form of dipeptidylpeptidase IV found in human serum. Isolation, characterization, and comparison with T lymphocyte membrane dipeptidylpeptidase IV (CD26). *J Biol Chem* (1995) 270: 14107-14.

Describes the purification of a large glycoprotein circulating in the serum that appeared to have dipeptidyl peptidase IV activity but was not CD26. In its denatured form, has a mass of approximately 175 kDa but non-denaturing gel chromatography suggests a molecular mass of 570 kDa implying a trimeric association in the absence of contaminating protein. The core peptide is around 135-140 kDa. A number of peptide sequences are identified that suggest a relationship to the EC3.4.-.- peptide hydrolases. The isolated protein is itself highly proteolytically-resistant. Unlike CD26, the enzyme activity is inhibited by EDTA and bestatin, a chymotrypsin-like serine proteinase inhibitor. This large soluble protein enhances the responses of peripheral blood leukocytes to recall

antigens but does not induce proliferation in its own right. All the evidence points to a DPPIV activity distinct from CD26, particularly since CD26 binds adenosine deaminase strongly but this new material does not. Labeling of the active site suggests that it may be a separate enzyme. Nevertheless, the question lingers as to whether this is truly a protease or whether there is a contamination with CD26, a highly potent enzyme that is not required in large amounts to yield a strong enzymic activity removing N-terminal dipeptides from chemokines/neuropeptides with a penultimate N-terminal proline.

1996

Duke-Cohan JS, Morimoto C, Rocker JA, Schlossman SF. Serum high molecular weight dipeptidyl peptidase IV (CD26) is similar to a novel antigen DPPT-L released from activated T cells. *J Immunol* (1996) 156: 1714-21.

Antibody directed against highly purified high molecular weight "serum DPPIV" strongly recognises CD26 despite no apparent contamination of the immunising preparation with CD26. Removal of the anti-CD26 activity results in an antibody that recognises not only the purified serum protein but also recognises a rapidly-upregulated and transient T cell activation antigen with strikingly different expression kinetics to those of CD26.The new antigen is named DPPT-L and it appears to be released by activated T cells. Like the circulating "large serum DPPIV", DPPT-L released from T cells is able to enhance the responses of peripheral blood leukocytes to recall antigens. The similar properties of large serum DPPIV and DPPT-L released from T cells suggest that one of the sources of the soluble form may be the activated circulating T lymphocyte. Nevertheless, DPPT-L is not lymphocyte-specific – it is found to be highly expressed on a large number of renal, pancreatic and hepatic carcinoma cell lines and expression correlates well with the likely secretory capacity of the original tissue types. The question then raised is whether the apparent membrane expression is due to a true trans-membrane protein or rather represents the a transient expression at the membrane of the soluble form as vesicles fuse and release their contents.

1997

Miller KA, Gunn TM, Carrasquillo MM, Lamoreux ML, Galbraith DB, Barsh GS. Genetic studies of the mouse mutations mahogany and mahoganoid. *Genetics* (1997) 146: 1407-15.

First evidence from genetic crosses of *mg/mg* with mice expressing high ectopic levels of agouti and with Mc1R-deficient mice (the Extension locus) that the product of the mahogany (*mg*) gene functions upstream of the melanocortin-1 receptor but downstream of agouti leading to the proposal that the mahogany product (and perhaps mahoganoid (*md*) product) modulate agouti interactions with Mc1R.