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Glycosylation of proteins and lipids by the cell has a profound influence on many aspects of the immune system and cell biology. We have manipulated carbohydrates on the surface of cells to reduce the rejection process in xenotransplantation (transplantation of tissues between species). Carbohydrates are synthesised by glycosyltransferases, located in the endoplasmic reticulum and Golgi apparatus, which catalyse the sequential transfer of

monosaccharides from nucleotide sugars to saccharide acceptors resulting in mature oligosaccharides. We have recently demonstrated that one of these transferases, iGb3 synthase (iGb3S), which is expressed in mice, rats and pigs, is not expressed in humans. This may have important consequences for xenotransplantation. This project will involve generating specific mutations in human iGb3S to determine which amino acid(s) are responsible for this inactivation.

Techniques:

Molecular Biology
FACS analysis
Western-blot
Cell culture
RT-PCR
UV microscopy

Projects

1. Identification of the specific amino acids in human iGb3S responsible for its inactivation

Publications:

Christiansen D, Mouhtouris E, Milland J, Zingoni A, Santoni A, Sandrin MS. Recognition of a carbohydrate xenoepitope by human NKR1A (CD161). *Xenotransplantation*; 13: 440–446, 2006.

Milland J, Christiansen D, Lazarus BD, Taylor SG, Xing PX and Sandrin MS. The molecular basis for Gal alpha(1,3)Gal expression in animals with a deletion of the alpha 1,3 galactosyltransferase gene. *J.Immunol.* 176:2448-2454, 2006.

Christiansen D, Milland J, Mouhtouris E, Vaughan H, Pellicci DG, McConville MJ, Godfrey DI, and Sandrin MS. Humans lack iGb3 due to the absence of functional iGb3-synthase: implications for NKT cell development, self-recognition and transplantation. *PLoS Biol.*15;6(7):e172, 2008.