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HUMAN STEM CELL DIFFERENTIATION IN VIVO FOLLOWING IN UTERO TRANSPLANTATION IN LARGE ANIMALS

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Abstract

The discovery of common placental circulation between twins coupled with the development of erythrocyte profiling in cattle allowed Ray Owen (Science 1945) to determine that dizygotic twins were chimeric with their sibling's blood cells after birth. Thus, he concluded that self-tolerance is acquired during fetal development by the intermingling of sibling cells via the placental circulation. Further, he concluded immune tolerance to self is not genetically determined or innate!! They have exploited this process to engraft human stem cells in a large animal (sheep) via in utero transplantation (IUT). Advantages to large animal investigation include long life span and large size to permit serial sampling. Using parallel serial studies in developing sheep fetuses stem cell engraftment receptivity and sheep lymphoid ontogeny were assayed longitutinally. Then they were able to identify an engraftment window and propose our antigen exposure model to explain acquisition of immune tolerance to self as chimeric animals display life-long immune tolerance to the graft. The subsequent chimeras yield human hematopoietic, islet, hepatic, cardiac and gastrointestinal cellular elements in situ. Circulating human proteins (IgM, Albumin, Factor VIII, C-peptide and ⍰-fetoprotein) are detected years after transplantation. Therefore, they believe a fully tolerant large animal host provides an ideal in vivo method to test human stem cell differentiation capacity. This presentation will discuss evidence for immune tolerance, the pivotal role of the thymus and potential advantages/controversies in assaying stem cell differentiation in vivo (in comparison to immune deficient animal models) following IUT. Limitations to stem cell differentiation following IUT will be discussed as well.

Biography

John S Pixley joined the faculty at Texas Tech University Health Science Center as the J T and Margaret Talkington Endowed Chair and Division Chief in Rheumatology/Immunology in 2015. Previously, he was at the University of Nevada School of Medicine as Division Chief of Rheumatology. His research over the past 20 years has focused on developing in utero transplantation as a scientific method and its poorly recognized capability to further understanding of Immune ontogeny of self-tolerance and Human stem cell pluripotency in vivo in a tolerant environment.

Publications

1. Comparison of once-daily captopril or enalapril in mild essential hypertension JS Pixley, MK Marshall, H Stanley, GH Starich… - The Journal of Clinical Pharmacology, 1989
2. A case of relapsing polyarthritis associated with hidradenitis suppurativa: case report and review of literature A Adiga, J Pixley - Journal of investigative medicine high impact case …, 2016
3. Absence of gender sensitivity to single dose streptozotocin in outbred mice JS pixley - Journal of investigative medicine, 2017
4. P15: relapsing erosive polyarthritis associated with hidradenitis suppurativa AG Adiga, JS Pixley – 2016
5. Comparison of angiotensin converting enzyme-activity in sera obtained by venipuncture versus fingerstick JS pixley, Rk Ferguson, MK Marshall… - Faseb Journal, 1988

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