James L Sherley, J Cell Sci Ther 2014, 5:4
http://dx.doi.org/10.4172/2157-7013.S1.028

OMICS Group Conferences
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4th World Congress on
Cell Science & Stem Cell Research
June 24-26, 2014 Valencia Conference Centre, Valencia, Spain

Probing the biological significance of non-random sister chromatid segregation in distributed stem cells

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Non-random sister chromatid segregation is a remarkable property of asymmetrically self-renewing distributed stem cells (DSCs). Unlike the expected randomization of sister chromatids with respect to template DNA age during mitotic chromosome segregation, mitosis by asymmetrically self-renewing DSCs results in the new DSC sister retaining all the chromosomes with the older template DNA strand. Reciprocally, the non-stem sister, whichis committed to producingthe tissue-specific differentiated cell lineage, receives the chromosomes with the younger template DNA strands. Non-random segregation was originally proposed as a molecular mechanism evolved to reduce the accumulation of detrimental mutations in tissue DSCs that are essential for normal vertebrate tissue function, renewal, and repair. More recently, withthe operation of non-random segregation now being described in several mammalian tissues, the mechanism has also been suggested as an important element of tissue developmental cell fate determination. In particular, proteins associated preferentially with the older "immortal" or the younger "mortal" template DNA strands may be important determinants of the DSC fateversusthe committed differentiating cell fate. Employing cultured DSC strains, we have begun a molecular dissection of regulatory histone features associated distinctlywith immortal versus mortal chromosomes. Our studies reveal intriguing asymmetries between the two sets of chromosomes in the level of detection of histone variants and histone modifications associated with gene activation and gene repression. In addition to providing new clues to the biological significance of non-random sister chromatid segregation, the newly discovered molecular asymmetries constitute new, specific biomarkers for detection and quantification of tissue DSCs.

Biography

James Sherley graduated from Harvard College (1980) and completed joint M.D./Ph.D. degrees at the Johns Hopkins University School of Medicine (1988). After post-doctoral studies at Princeton University, beginning in 1991 he lead cancer cell molecular biology research at Fox Chase Cancer Center. In 1998, he began adult stem cell research at Massachusetts Institute of Technology, and in 2007 continued at Boston Biomedical Research Institute. In 2013, he founded the Adult Stem Cell Technology Center, LLC, (ASCTC), which he currently directs. ASCTC is developing technologies for mass-producing human tissue stem cells for applications in drug development and transplantation medicine. Honors & Awards 2006 NIH Director's Pioneer Award 2003 Ellison Medical Foundation Senior Scholar Award in Aging Research 1993 Pew Scholar Award in Aging Research 1993 Pew Scholar Award in the Biomedical Sciencesthe Biomedical Sciences.

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