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Stem cells, cancer stem cells: Differentiation, division and death

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In 2003 a novel type of cell displaying both symmetric and asymmetric divisions, shibboleths of stem cells that must both drive net growth and give rise to differentiated cells were discovered. The cells were neither prokaryotic or eukaryotic and was known as metakaryotic cells. Metakaryotic cells have large, hollow, bell shaped nuclei displaying bizarre modes of amitotic (non-mitotic) nuclear division, genomic organization, DNA segregation and synthesis. For instance, whether dividing symmetrically or asymmetrically they first form double-stranded RNA/DNA helices from opposite strands of each maternal and paternal chromatid sequence. These are segregated into daughter cells and then the RNA is degraded and the double stranded DNA helix is restored by direct copying. Between cell divisions the parental homologs appear to be paired and end-joined at the telomeres to other homologously paired chromatids. Metakaryotic stem cells re-appearing in adenocarcinomas display as mononuclear cells. Metastases, however, display the metakaryotic tubular syncytia found in early fetal development of weeks ~4-12. In terms of growth rates and histologic organization of metakaryotes and crypt-like structures, adenoma resemble pediatric tissue. Adenocarcinomas resemble tissues of ~16-24 weeks. Metastases recall the earliest fetal period 4-12 weeks of gestation. In these observations of metakaryotic stem cells, the arguments of Virchow and Cohnheim circa 1876 that tumors' histologic organization and growth rates were similar to that of developing fetal tissues was confirmed and extended. Studies suggest instead adenomatous lesions arise from metakaryotic stem cell mutations limited to the fetal/juvenile period but are detected in adults after many decades of steady growth and final transformation of a single precancerous metakaryotic stem cell into a cancer stem cell. Recently similar behavior in another putatively clonal disease, atherosclerosis was found. The phenotype of smooth muscle cells in plaque neointima and post-surgical restenoses had also been described by pathologists as 'immature' or 'juvenile', and myofibroblasts of plaques first appeared after fetal/juvenile angiogenesis was completed and outgrowths became apparent. Since 2011, several approaches to nominate agents that might be 'metakaryocidal' and thus possibly useful in treating tumors and atherosclerotic plaques by targeting cancer and atherosclerosis stem cells. Both were envisioned as stem cell targeting drugs and as tools of exploration of fundamental mechanisms evolved in stem cell physiology. The motive behind the work is to re-explore John Cairn's hypothesis of immortal DNA strands in maintenance stem cells and understand the role of non-random segregation of genomic elements in specifying the organisms' developmental program as expressed in metakaryotic stem cells.

Biography

Elena Gostjeva completed her PhD from Vavilov's Institute of Genetics, Moscow, Russia in 1986. Then she immediately was enrolled into studies of genetic risk assessment at Chernobyl Radiobiological Expedition headed by Institute of Evolutionary Morphology and Ecology of Animals at USSR Academy of Sciences. In 1994, after collapse of Soviet Union she was appointed as the Head of the group 'Genetic Risk Assessment of Chernobyl Fallout' at Kiev Polytechnical Institute, Ukraine. She conducted her research in Ukraine in collaboration with Prof. Lars Ehrenberg at the University of Stockholm and Swedish Radiation Protection Institute. In 1997, she joined MIT, USA working on mutational spectrometry applied in measuring mutations in human tissues. In 2003, after discovery of metakaryotic stem cells and up to date she continues to work at MIT under sponsorship of 'United Therapeutics' Inc. She has published 7 original papers in stem cells and cancer research and has 7 patents, 2 granted in the areas of stem cells in development, cancer, wound healing, atherosclerosis, organ transplant restenosis, veterinary as well as patents in drugs and regiments to target cancer stem cells.

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