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CCR5 Governs stem cell characteristics, therapy resistance and metastasis of breast and prostate cancer

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Tumor initiating cells convey stem-like features and contribute to therapeutic resistance and tumor metastases. Cancer stem cells are protected against chemotherapy- and radiotherapy- induced death, through mechanisms that protect genomic integrity via induction of DNA damage sensing and DNA repair machinery. In mammalian cells, double-stranded breaks (DSB) may be repaired by either homology directed recombination (HDR), or non-homologous end joining (NHEJ) and single-strand annealing (SSA). Defects in these repair mechanisms can result in chromosomal fusions, translocations and breaks. The molecular mechanisms linking cancer stem cells and DNA repair are poorly understood. Herein, the chemokine receptor CCR5, which is known to contribute to breast cancer progression and metastasis, was shown to promote stem cell-like properties and enhance DNA repair. Reintroduction of CCR5 into CCR5-negative cells promoted breast tumor stem cell expansion, metastases, and the induction of DNA repair gene expression. CCR5 was shown to enhance the repair of DSBs by inducing HDR and SSA-based DNA repair. The finding that CCR5 on cancer cells augments DNA repair and cancer stem cell expansion suggests CCR5 inhibitors may enhance the tumor specific activities of DDR-based treatments. (Up to 250 words)

Biography

Professor Pestell completed his MBBS and subsequently PhD, M.D., (Melbourne University) FRACP, FACP, MBA (NYU) with post-doctoral studies at Harvard University and Massachusetts General Hospital. He was Director of the Lombardi Comprehensive Cancer Center, the Sidney Kimmel Cancer Center and most recently Executive Vice President of Thomas Jefferson University. He is the author of over 620 published works and 36 books and chapters, with over 45,700 citations, H index 115. He served and or serves on 14 scientific journal editorial boards, external advisory boards of 7 NCI cancer centers, several international research institutes, and review boards for research funding agencies of USA, Italy, UK, Switzerland, Ireland, France, Israel, Australia, and Czech. He is the founder of two biotechnology companies, has multiple issued patents and is a member of National Academy of Inventors (Jefferson Chapter).

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