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### **CCR5 governs stem cell characteristics, therapy resistance and metastasis of breast cancer**

Recent studies have demonstrated a propensity of tumor initiating cells with stem cell-like features to contribute to metastasis and therapy resistance. The mechanisms by which cancer stem cells survive chemotherapy- and radiotherapy is not well understood. We herein describe the novel finding that the immune chemokine receptor CCR5 is selectively expressed on transformed breast epithelial cells, promoting breast cancer stem cell expansion and DNA damage 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 Double Stranded DNA Breaks (DSBS) by inducing HDR and SSA-based DNA repair. Single cell sequencing documented activation of gene expression pathways mediating ribosomal biogenesis and cell survival in CCR5<sup>+</sup> cells. In a broad array of BRCA1 mutant breast cancer cell lines DNA damaging chemotherapeutic agent mediated cell killing was dramatically enhanced by CCR5 antagonists. Because CCR5 is expressed only on the breast cancer epithelial cells the current findings illustrate CCR5 inhibitors enhance the tumor specific activities of DDR-based treatments.

### **Biography**

Richard George Pestell completed his MBBS and subsequently PhD, MD (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 (2002-2005), the Sidney Kimmel Cancer Center (2005-2015) 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 50,000 citations, H index 121. 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 and has multiple issued patents.

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