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Embryonic NANOG activity defines colorectal cancer stem cells and modulated through AP1- and TCF-dependent mechanisms

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Understanding the mechanisms of cancer stem cell regulation is required to ensure their safe use in clinical applications. Embryonic NANOG (NANOG1) is considered as an important regulator of pluripotency while NANOGP8 (NANOG-pseudogene) plays a role in tumorigenesis. Herein, we show NANOG is expressed from both NANOG1 and NANOGP8 in human colorectal cancers (CRC). Enforced NANOG1-expression increases clonogenic potential and tumor formation in xenograft models, although it is expressed only in a small subpopulation of tumor cells and is colocalized with endogenous nuclear β-catenin^{High}. Moreover, single NANOG1-CRCs form spherical aggregates, similar to the embryoid body of embryonic stem cells (ESCs), and express higher levels of stem-like Wnt-associated target genes. Furthermore, we show that NANOG1-expression is positively regulated by c-JUN and β-catenin/TCF4. Ectopic expression of c-Jun in murine Apc^{Min}-ESCs results in the development of larger xenograft tumors with higher cell density compared to controls. Chromatin immunoprecipitation assays demonstrate that c-JUN binds to the *NANOG*1-promoter via the octamer *M*1 DNA element. Collectively, our data suggest that β-Catenin/TCF4 and c-JUN together drive a subpopulation of CRC tumor cells that adopt a stem-like phenotype via the *NANOG*1-promoter.

Biography

Abdol Rahman Shams Nateri completed his doctorate in genetics engineering at the Essex Univ. 2002, he joined LRI (ICRF), where he carried out a research combining basic-research into the cellular/molecular biology of cancer-genomics with translational research. His endless passion in cancer-biology and, his excellent achievements, boast publications in Nature, Science, etc. Dr Nateri joined the faculty of the Nottingham Univ, in 2007, where he is an Associate Professor and established the Cancer Genetics & Stem Cell laboratory. As the lab name states, the group focused on cancer genetics and stem cells mechanisms using prestigious cancer mouse and neoplastic stem cell models.