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Integrin $\alpha 1\beta 1$ overexpression confers pro-proliferative and pro-migratory advantage to colorectal cancer tumours

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Being one of the leading causes of death from cancer in western countries, colorectal cancer (CRC) needs to be better understood to improve treatment. In the small intestine the $\alpha 1$ integrin subunit is present only in proliferating crypt cells while its exclusive partner $\beta 1$ is constitutively expressed in all intestinal cells supporting a reported role for $\alpha 1$, via caveolin-1 and Shc, in the downstream activation of the Ras/ERK proliferative pathway. In mouse models, the $\alpha 1\beta 1$ integrin supports breast cancer cell motility and, together with the Kras oncogenic factor, potentiates tumour growth. We postulated that integrin $\alpha 1\beta 1$ is highly expressed in CRC and has a protumoral effect related to $\alpha 1$ subunit expression and regulation. Results: Immunofluorescence showed $\alpha 1$ only at the basolateral domain of proliferative crypt cells in the normal colon mucosa. Immunohistochemistry analysis performed on a tissue microarray containing 65 adenocarcinomas and their matched margins showed $\alpha 1$ to be highly expressed in 57% of tumours compared to margins, correlating with $\alpha 1$ mRNA levels. Interestingly, $\alpha 1$ overexpression was present in the early stages of CRC. In the colorectal HT29 and SW480 tumour cell lines, $\alpha 1$ mRNA silencing resulted in reduced cell proliferation (52% and 54% respectively) and migration compared to the control. Our results show that $\alpha 1\beta 1$ is significantly over-expressed in CRC and is implicated in tumour progression. We are currently working on the regulation of the $\alpha 1$ sub unit, which could be a potential therapeutic target in the treatment of CRC. Supported by CIHR.

Biography

Salah Boudjadi completed his residency in pathology at the University of Reims (France). His training was focused on the pathology of the gastrointestinal tract. Then he performed, at the University Paris 7, an internship in cytopathology of different organs including the liver and the pancreas. Thereafter, he followed a career in cancer research at the University of Sherbrooke, Canada. Currently he works on the regulation and function of various membrane proteins involved in colorectal cancer. He obtained grants from the Centre de recherches sur la biologie des épithéliums and from the Centre d'excellence of the University of Sherbrooke.

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