

New role for Vascular Endothelial Growth Factor in regulating skin cancer stem cells

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Skin squamous cell carcinomas are amongst the most frequent cancers in humans. Recent studies suggest that skin squamous cell carcinoma, like many other human cancers, contain particular cancer cells, known as cancer stem cells, that present increased self-renewal potential that sustain tumor growth. Little is known about the mechanisms that regulate cancer stem cell functions.

To dissect the mechanisms that regulate cancer [stem cells](#), the researchers determined which genes are preferentially expressed by cancer stem cell of skin tumors. They found that VEGF, a molecule known to regulate the formation of new vessels, is expressed at high level by skin cancer stem cells, which are located in close contact to the blood vessels. Administration of an antibody that decreases new [blood vessel formation](#) to mice presenting [skin tumors](#) results in a reduction of the pool of cancer stem cells leading to a reduction of the tumor size, demonstrating that vascular cells regulates skin cancer stem [cell functions](#).

To determine whether VEGF secretion by cancer stem cells directly regulates the function of cancer stem cells, the authors genetically removed VEGF specifically in [tumour cells](#), and found that upon VEGF ablation, skin cancer stem cells are rapidly lost due to a defect in their renewal properties, leading to tumour regression.

"It was extremely exciting to see the complete disappearance of these tumors only two weeks after the treatment" said Benjamin Beck, the first author of the *Nature* paper.

The authors also found that Neuropilin 1, a VEGF receptor, is also highly expressed by skin cancer stem cells, and showed that Neuropilin 1 expression by cancer stem cells is critical to promote cancer stem cell renewal and tumour growth. In addition, the authors found that Neuropilin 1 is also essential for tumour formation,

demonstrating the critical role of Neuropilin 1 during both cancer initiation and tumor growth.

Altogether this new study provides novel and important insights into the mechanisms by which VEGF controls tumour growth. VEGF signalling in endothelial cells is critical to sustain the formation of the vascular niche, promoting indirectly the renewal of skin cancer stem cells. VEGF secretion by cancer stem cells acts also directly on cancer stem cells by a Neuropilin 1 dependent mechanism to promote cancer stem cell renewal and tumor growth.

"Anti-VEGF therapies are currently used to treat cancers. These new results have important implications for the prevention and treatment of different epithelial cancers, as new therapies blocking VEGF and/or Neuropilin 1 functions in [cancer cells](#) may be more effective for the treatment of certain cancers compared to the therapeutic strategies blocking VEGF function only in endothelial cells" said Cédric Blanpain, the senior and corresponding author of the *Nature* paper.

In conclusion, this new study, published in the online early edition of *Nature*, identifies a dual role for VEGF in regulating skin cancer stem cells and tumor progression.

More information: Beck B et al, The vascular niche and a VEGF/Nrp1 loop regulates the initiation and stemness of skin tumours, *Nature*, 2011, [doi:10.1038/nature10525](https://doi.org/10.1038/nature10525)

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