

## Interactions between cancer stem cells and their niche govern metastatic colonization

**Ilaria Malanchi**

*London Research Institute, Cancer Research UK*

*London Research Institute*

*44 Lincolns Inn Fields London WC2A 3LY*



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Metastatic growth in distant organs is the major cause of cancer mortality. We have now identified two key mechanisms essential for the initiation of metastasis: first, a small population of cancer stem cells (CSCs) that is critical for metastatic colonization. These CSCs represent a stable population of tumour cells which selectively survive and proliferate upon metastatic seeding and thereby drive the initial expansion of cancer cells at the secondary site. In contrast, non-CSCs fail to grow, are rapidly lost and do not de-differentiate into CSCs *in vivo*.

Second, we find stromal niche signals to be crucial for this process. We identify the extracellular matrix (ECM) component POSTN to be expressed by fibroblasts in the normal tissue and in the stroma of the primary tumour. Importantly, infiltrating tumour cells need to induce stromal POSTN expression in the secondary target organ to initiate colonization. This ECM protein is required to allow cancer stem cell maintenance and blocking POSTN function prevents metastasis. POSTN recruits Wnt ligands and thereby increases Wnt signalling in cancer stem cells.

We suggest that the education of stromal cells by infiltrating tumour cells is an important step in metastatic colonization and that preventing de-novo niche formation may represent a novel treatment strategy against metastatic disease.

### References

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**Ilaria Malanchi**

Tumour Host Interaction Lab  
Cancer Research UK London Research Institute  
44 Lincolns Inn Fields London, WC2A 3LY  
Tel. +44 (0)20 7269 3168 Fax. +44 (0)20 7269 3094  
Website: <http://www.london-research-institute.org.uk/research/ilaria-malanchi>

**EDUCATIONS/TRAINING**

1998 Siena University MSc Biology  
2002 Heidelberg University PhD Dr.rer.nat.  
2003-2004 IARC, WHO, Lyon Postdoc Infection and Cancer  
2004-2011 ISREC, EPFL, Lausanne Postdoc Cancer stem cell laboratory

**POSITIONS AND HONORS**

2004-2011 Research Scientist, ISREC, EPFL, Lausanne Switzerland  
2011-present Group Leader, Tumour Host Interaction Lab, Cancer Research UK, London, UK

**RECENT PUBLICATIONS**

1. Malanchi I, Santamaria MA, Susanto E, Peng H, Lehr HA, Delaloye JF, Huelsken J. "Interactions between cancer stem cells and their niche govern metastatic colonization" *Nature*. 481:85-89, 2012.
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