



Universiteit
Leiden
The Netherlands

The diverse roles of integrin $\alpha 3 \beta 1$ in cancer: Lessons learned from skin and breast carcinogenesis

Ramovš, V.

Citation

Ramovš, V. (2021, February 18). *The diverse roles of integrin $\alpha 3 \beta 1$ in cancer: Lessons learned from skin and breast carcinogenesis*. Retrieved from <https://hdl.handle.net/1887/3135050>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3135050>

Note: To cite this publication please use the final published version (if applicable).

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/3135050> holds various files of this Leiden University dissertation.

Author: Ramovš, V.

Title: The diverse roles of integrin $\alpha\beta1$ in cancer: Lessons learned from skin and breast carcinogenesis

Issue date: 2021-02-18

PROPOSITIONS

1. The role of integrin $\alpha\beta 1$ in cancer can only be understood when time and place are considered: nature of the cell environment (such as extracellular matrix composition), type of cancer and its driving mechanism, as well as the stage of the disease. – *this thesis*
2. Integrin $\alpha\beta 1$ exerts functions beyond mediating the adhesion of epithelial cells to laminin-matrix; however, it might be shortsighted to call all such roles adhesion independent. – *this thesis*
3. During the development of skin papillomas, integrin $\alpha\beta 1$ plays several roles, all of which are likely connected or even co-dependent: it mediates the strength of adhesion of basal keratinocytes to the basement membrane, modulates cell secretome, orchestrates signaling in basal and suprabasal keratinocytes and affects keratinocyte differentiation. – *this thesis*
4. The role of integrins in cell-cell contacts is underappreciated and deserves more attention. – *this thesis*
5. The choice of the cell culture model can have unprecedented consequences: the significant differences in PI3K-Akt-mTOR signaling cascade in a three dimensional versus two dimensional model demonstrates that it can severely affect even most commonly mutated signaling pathways in cancer. – *Riedl et al., 2017. J Cell Sci. 130: 203-218.*
6. Hair follicle has a unique ability to cope with Ras-activated cells: it is able to integrate the mutant epithelial cells while remaining clinically normal. However, follicular epithelial *Hras*-activation can activate the surrounding mesenchyme through alterations to both molecular signatures and cellular behaviors. – *Pineda et al, 2019. J Cell Biol.: 218(10):3212-3222.*
7. Integrin $\alpha\beta 1$ -dependent paracrine signals from tumor keratinocytes may contribute to a tumor-supportive microenvironment. – *Longmate et al. 2020. J Invest Dermatol.: S0022-202X(20)31584-0*

8. Considering the breadth of new evidence describing ECM ligand-independent integrin signaling in cancer cell survival and drug resistance, there may be a need to develop alternative strategies that exploit tumor-specific integrin expression profiles or downstream integrin effectors rather than focusing directly on interfering with integrin-ligand interactions. – *Hamidi and Ivaska, 2018. Nat Rev Cancer 18 (9): 533-548.*
9. “Science is not about building a body of known ‘facts’. It is a method for asking awkward questions and subjecting them to a reality-check, thus avoiding the human tendency to believe whatever makes us feel good.”
– *Terry Pratchett, The Science of Discworld*
10. Sometimes scientists change their minds. New developments cause a rethink. If this bothers you, consider how much damage is being done to the world by people for whom new developments do not cause a rethink. – *Terry Pratchett, The Science Of Discworld*
11. “Don’t aim at success. The more you aim at it and make it a target, the more you are going to miss it. For success, like happiness, cannot be pursued; it must ensue, and it only does so as the unintended side effect of one’s personal dedication to a cause greater than oneself or as the by-product of one’s surrender to a person other than oneself.” – *Viktor E. Frankl, Man’s Search for Meaning*
12. Maybe the best way to describe how my PhD journey felt mid-way is through the words of Terry Pratchett: “He’d been wrong, there was a light at the end of the tunnel, and it was a flamethrower.” (*Terry Pratchett, Mort*). Luckily, it turns out that J. R. R. Tolkien has been right all along: “Not all those who wander are lost.” (*J.R.R. Tolkien, The Fellowship of the Ring*)