Mechanisms of Ewing sarcoma metastasis : biochemistry and biophysics

Beletkaia, E.

Propositions

accompanying the thesis

Mechanisms of Ewing Sarcoma Metastasis
Biochemistry and Biophysics

1. Regulation of CXCR4 dynamics on the plasma membrane is controlled via cross-talk of G-protein dependent and independent pathways.

   Chapter 2 of this thesis

2. CXCR4 activates the G-proteins in a sequential manner, which in turn ensures faithful receptor signaling.

   Chapter 3 of this thesis

3. The application of optogenetic tools for the study of GPCRs requires extra precaution in sample preparation and handling, and yet has to be improved.

   Chapter 4 of this thesis

4. Mechanical properties of the microenvironment potentially act as additional cue leading Ewing sarcoma to its metastatic niche.

   Chapter 5 of this thesis

5. The initial amplification step in chemotactic signaling in Dictiostelium discoideum, which has been found as being controlled by receptor diffusion, is not ubiquitous among the chemotaxis in other systems.

   de Keijzer S. et al., J. Cell Sci. **121**, 1750-7 (2008)
   Chapter 2 and 3 of this thesis

6. Receptor mobility is a core regulation parameter for the fine control of receptor activity. Therefor, the studies of the receptors mobility on the plasma membrane deserve closer attention.
   Veya L. et al., J. Biol. Chem. (2015) and *Chapter 2 of this thesis*

7. The commonly used energy transfer methods (FRET and BRET) for studying GPCR dimerization, reflect the distance between the fluorophores rather than that of the receptors. In light of that, the results obtained by those techniques might require additional control experiments.
   Gurevich V. V. et al., Trends Neurosci. **31**, 74-81 (2008)

8. Pharmacological inhibitors are frequently used to test functional dependencies in cells. The scientific community realised that those may have various off-target effects, such that results should be taken with care. Although biological side effects have been variously addressed [Dutta, Kwik], side effects on physical properties like viscosity and diffusion have been neglected so far. Those physical effects, as being systemic, might turn out to be even more relevant to be addressed.
   Dutta et al., PLoS ONE **7**, e45799 (2012)
   Kwik et al., PNAS **100**, 13964-9 (2003)

9. Some negative results and failed protocols are more valuable than a success story. Thus, those should be shared equally.

10. A scientific evaluation should be based on the research quality, rather than the rank of the journal in which the research was published.

Elena Beletkaia
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