

Institution: **Ecole Polytechnique**

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Required background of the student: PhD in **Biology**

Funding: to be found together with the applicant

Isolation of novel tumor suppressor genes that monitor the actin cytoskeleton

Polymerization of branched actin by the Arp2/3 complex drives membrane protrusion during cell migration. In this process, the Arp2/3 complex is activated by the WAVE complex and inhibited by Arpin, which we have recently discovered. In most invasive tumors in the breast, there is either up-regulation of the WAVE complex or down-regulation of Arpin. These alterations are associated with a poor prognosis for breast cancer patients. We have shown that this signaling pathway controls cell migration and proliferation in a coordinated manner. To identify the genes that monitor the actin cytoskeleton, we have performed a genome-wide RNAi screen and found about 15 potential tumor suppressor genes, which allow cells arrested in their cell cycle by Arp2/3 inhibition to resume cell cycle progression. The goal of this post-doc project is to validate some of these candidates.

To this end, the post-doc will perform a secondary screen by obtaining KO of these genes in an immortalized human breast cell line or a breast tumor cell line, using the CRISPR-Cas9 technology. The positive hits that transform the immortalized line and renders the tumor cell line invasive will be further studied. We will address the localization of these tumor suppressor genes and their cellular function. We expect the hits to localize to the branched actin networks of membrane protrusions and to regulate cell migration. We will look for protein partners of the hits using proteomics in order to understand how they perform their function and how they are regulated.

5 representative publications of the group:

1. Lomakina ME, Lallemand F, [...], Bièche I, Alexandrova AY, Gautreau A. 2016. Arpin down-regulation in breast cancer is associated with poor prognosis. ***Brit J Cancer*** 114 :145-63.
2. Gorelik R, Gautreau A. 2015. The Arp2/3 inhibitory protein Arpin induces cell turning by pausing cell migration. ***Cytoskeleton*** 72:362-71.
3. Krause M, Gautreau A. 2014. Steering cell migration: lamellipodium dynamics and the regulation of directional persistence. ***Nature Review Mol Cell Biol*** 15:577-90.
4. Gorelik R, Gautreau A. 2014. Quantitative and unbiased analysis of directional persistence in cell migration. ***Nature Protocols*** 9:1931-43.
5. Dang I, Gorelik R, Sousa-Blin C, [...], Faix J, Blanchoin L, Gautreau A. 2013. Inhibitory signalling to the Arp2/3 complex steers cell migration. ***Nature*** 503:281-4.