**The NANOTUMOR Consortium**
https://www.nanotumor.fr/

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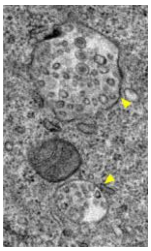
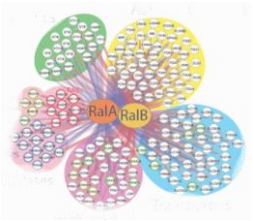


# Open position: New pathways in endosome formation and extracellular vesicle secretion in metastasis




The **NANOTUMOR consortium** is a French national multi-disciplinary workforce that aims to study cancer initiation and progression at molecular and subcellular level, by combining cutting-edge technologies in various cellular and animal models. In the context of preliminary results obtained within the consortium, the **Jacky G. Goetz** Lab at CRBS together with **Patrick Schultz** Lab at IGBMC are seeking a **dedicated postdoctoral scientist** with background in **Cell Biology, Microscopy and Cancer Biology**.

## Environment

Work in the **Goetz lab** aims at understanding the cellular and subcellular mechanisms driving metastasis in relevant and controlled animal models, namely mouse and zebrafish (Goetz et al., 2011, 2014; Follain et al., 2018; Hyenne et al., 2019; Osmani et al., 2019 Ghoroghi et al., 2021). Over the past years, they investigated the contribution of tumor extracellular vesicles as well as mechanical forces in metastasis onset. They recently described the role of RAL GTPases in the biogenesis of multivesicular bodies and exosome secretion, and their subsequent roles in metastasis formation (Ghoroghi et al. 2021). Work in the **Schultz lab** is focused on the molecular mechanisms that control gene expression at the transcription initiation level. The structure of several multiprotein complexes such as transcriptional coactivators, general transcription factors and chromatin remodelers have been determined by single particle cryo electron microscopy (Sharov et al., 2017, Kolesnikova et al., 2018, Papai et al., 2020). The long-term objective is to study the localization, the structure and the molecular environment of these transcription factors in the context of the cell nucleus. The team implemented cellular electron tomography (Kizilyaprak et al., 2010), live cell immune gold labelling (Orlov et al., 2015), FIB-SEM imaging (Hoang et al., 2017, Spehner 2020) and milling to apply a multi-resolution structural approach. To extract quantitative volumetric information, the team also contributed to develop segmentation methods (Hoang et al., 2017) based lately on deep learning approaches (Meyer et al., 2020). he Goetz lab has recently relocated into the **Center for Biomedical Research of Strasbourg (CRBS)**, a new institute that is equipped with multiple platforms and facilities (mouse and zebrafish husbandry, imaging facility, sequencing platform). The Schultz lab is located at **IGBMC (Illkirch)** and has full access to state of the art **photonic and electron microscopy equipment.**

## Project

The project proposed here aims to characterize the **function of newly identified proteins in endosome formation and dynamics as well as in extracellular vesicle secretion (and metastasis)**. These proteins were recently identified as new partners of RAL GTPases by proximal interactome and co-immunoprecipitation within the NANOTUMOR consortium. **The selected candidate will use a combination of cell engineering, cell biology, proteomic analysis and volumetric imaging and animal experiments to probe the role of recently identified proteins. In particular, 3D electron microscopy (FIB-SEM) will be used to characterize endosomal phenotypes at nanoscale resolution.**

The successful candidate will join an interdisciplinary team made of cell and cancer biologists, molecular biologists and physicist. The candidate will develop his project autonomously but in close collaboration with another post-doctoral fellow, under the close supervision of Vincent HYENNE (Extracellular vesicles), Jacky GOETZ (Metastasis) and Patrick Schultz (Electron microscopy). The project will benefit from the multidisciplinary **NANOTUMOR consortium** to access multiple expertises, and in particular in proteomics (E.Coyaud/I.Fournier (PRISM, Lille) and A.Daulat/J.P. Borg (CRCM, Marseille)) but also micropatterning and fluorescent imaging. The candidate is also expected to present his results in the form of publications and international conference presentations, and to participate to writing of grant applications.

**For more information** on the group's research: J. G. Goetz Team & P. Schultz Team

**Applications must be sent to:** J. G. Goetz (jacky.goetz@inserm.fr) and P. Schultz (pat@igbmc.fr)

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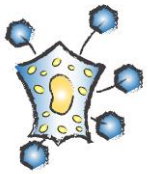

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**About the candidate**

**Skills (recommended but not mandatory)**

- Strong experience in cell and organelle biology. Extracellular vesicle biology would be a plus
- Experience with electron microscopy (sample preparation and handling, imaging, segmentation)
- Experience in both light & electron microscopy would be **a very significant asset** (FIB-SEM)
- Cell engineering (CRISPR, lentivirus, siRNA..)
- Good experience with photonic microscopy (confocal, spinning-disk or 2PEM)
- Experience with Image analysis softwares
- Ability to work independently and collaboratively with biologists and physicists in the team
- Being a team player, organized and curious, and able to drive the dynamics of the project
- Good communication and writing skills
- Fluency in English (lab comp. of people from France, Spain, Argentina, Czech Republic, India...)

**Please include the following in your application:**

- A cover letter
- Your resume including at least 2 referees with supporting letters/contact details

**Contract:** The position is an initial full time one-year contract with strong prospects for renewal. The salary will be adapted to the experience of the candidate. The candidate will apply to additional funding (at national and European level). **For this purpose, we are interested in candidates who recently defended their *Ph.D.* (early post-doctoral fellow).**

**This position will remain open until filled.**

We are reviewing applications as they are received:
as such candidates are encouraged to **submit their application as soon as possible**.

Starting date: **as soon as possible**

## Relevant bibliography:

### Goetz team

Ghoroghi, S., et al. (2021). Ral GTPases promote breast cancer metastasis by controlling biogenesis and organ targeting of exosomes. ***ELife***, *10*.

Goetz, J. G., et al. (2011). Biomechanical Remodeling of the Microenvironment by Stromal Caveolin-1 Favors Tumor Invasion and Metastasis. ***Cell***, *146*(1), 148–163.

Goetz, J. G., et al. (2014). Endothelial Cilia Mediate Low Flow Sensing during Zebrafish Vascular Development. ***Cell Reports***, *6*(5), 799–808.

Hyenne, V., et al. (2019). Studying the Fate of Tumor Extracellular Vesicles at High Spatiotemporal Resolution Using the Zebrafish Embryo. ***Developmental Cell***, *48*(4), 554-572.e7.

Karreman, M. A., et al. (2016). Intravital Correlative Microscopy: Imaging Life at the Nanoscale. ***Trends in Cell Biology***, *26*(11), 848–863.

Karreman, M. A., et al. (2014). Correlating Intravital Multi-Photon Microscopy to 3D Electron Microscopy of Invading Tumor Cells Using Anatomical Reference Points. ***PLoS ONE***, *9*(12), e114448.

Osmani, N., et al. (2019). Metastatic Tumor Cells Exploit Their Adhesion Repertoire to Counteract Shear Forces during Intravascular Arrest. ***Cell Reports***, *28*(10), 2491-2500.e5.

Follain, G., Osmani, N., et al. (2018). Hemodynamic Forces Tune the Arrest, Adhesion, and Extravasation of Circulating Tumor Cells. ***Developmental Cell***, *45*(1), 33-52.e12.

### Schultz team

Sharov, G. *et al.* Structure of the transcription activator target Tra1 within the chromatin modifying complex SAGA. *Nature communications* 8, 1556 (2017).

Hoang, T. V., Kizilyaprak, C., Spehner, D., Humbel, B. M. & Schultz, P. Automatic segmentation of high pressure frozen and freeze-substituted mouse retina nuclei from FIB-SEM tomograms. *Journal of structural biology* 197, 123-134 (2017)

Orlov, I. *et al.* Live cell immunogold labelling of RNA polymerase II. *Sci Rep* 5, 8324 (2015).

Kolesnikova, O., A. Ben-Shem, J. Luo, J. Ranish, P. Schultz and G. Papai (2018). "Molecular structure of promoter-bound yeast TFIID." Nat Commun 9(1): 4666.

Papai, G. *et al.* Structure of SAGA and mechanism of TBP deposition on gene promoters. *Nature* **577**, 711-716, (2020).

Meyer C, Mallouh V, Spehner D, et al. Automatic multi class organelles segmentation for cellular FIB-SEM images. *Int Symp Biomed Imaging (ISBI), IEEE*. Published online April 2021:668–672. Accessed October 26, 2021. https://hal.archives-ouvertes.fr/hal-03238132

Kizilyaprak, C., Spehner, D., Devys, D. & Schultz, P. In vivo chromatin organization of mouse rod photoreceptors correlates with histone modifications. *PloS one* **5**, e11039, (2010).

Spehner D, Steyer AM, Bertinetti L, et al. Cryo-FIB-SEM as a promising tool for localizing proteins in 3D. *J Struct Biol*. 2020;211(1):107528. doi:10.1016/j.jsb.2020