



A postdoctoral fellow position is available at the University of Bern, Switzerland, to join the research group of Sven Rottenberg (Vetsuisse Faculty and Bern Center for Precision Medicine).

## Postdoctoral fellow position to study replication fork biology in the context of chemoresistance

Our laboratory studies mechanisms of anti-cancer therapy resistance with a special focus on alterations in the DNA damage response (DDR). Most cancers have lost critical DDR pathways during tumor evolution. This provides a useful explanation for the initial sensitivity of tumors to DNA-targeting therapy. A striking example is dysfunctional homologous recombination (HR), *e.g.* due to inactivating mutations in the *BRCA1* and *BRCA2* genes. Extensive efforts are being made to develop novel targeted therapies exploiting such HR defects. Inhibitors of poly(ADP-ribose) polymerase (PARP) are an instructive example of this targeted therapeutic approach. Despite the success of PARP inhibitors, the presence of primary or acquired therapy resistance remains a major challenge in clinical oncology. To move the field of precision medicine forward, we need to understand the precise mechanisms causing therapy resistance. In recent years, restored replication fork (RF) stability has been put forward as crucial process to explain poor drug response. In fact, some factors involved in DNA double-strand break repair have independent functions in RF biology and their loss causes fork degradation and therapy sensitivity. However, when cells find alternative ways to stabilize the RFs, drug resistance can develop. By studying the underlying mechanisms, we expect to find new insights into the interplay between the DDR and the replication machinery.

**In the scope of this postdoc position**, we intend to develop a variety of advanced biochemical, proteomic and genetic approaches to understand the effects of RF alterations on chemoresistance. We are particularly interested in identifying novel factors that protect RFs or consolidate fork reversal and subsequent restart. Moreover, we search for therapeutic approaches to circumvent or reverse resistance. To this purpose, we use various model systems, including unique *BRCA1/2*-deficient 2D cell lines and 3D cancer organoids as well as genetically engineered mouse models for hereditary breast cancer.

**We are looking for** a highly motivated candidate with a solid background in biochemistry, molecular biology and cell biology. You should have a strong interest in linking basic biology to anti-cancer therapy resistance.

**We offer** a young and enthusiastic research group, an inspiring research environment, state-of-the art research facilities at the attractive working location in Bern. The remuneration is in accordance with the Swiss National Science Foundation (SNSF) regulations (annual brutto salary of CHF 80,000 - 105,000).

This position is a 3-4 year appointment and is available from March 1<sup>st</sup>, 2021.

**How to apply:** please send your application as a single pdf document including a motivation letter, CV and references (letters or contact information of two references) by email to Christine Herzig ([christine.herzig@vetsuisse.unibe.ch](mailto:christine.herzig@vetsuisse.unibe.ch)). For questions regarding the position, please contact Prof. Sven Rottenberg ([sven.rottenberg@vetsuisse.unibe.ch](mailto:sven.rottenberg@vetsuisse.unibe.ch)). More information about the Rottenberg group you find under [www.itpa.vetsuisse.unibe.ch/research/therapy\\_escape\\_of\\_cancer](http://www.itpa.vetsuisse.unibe.ch/research/therapy_escape_of_cancer) and about the Bern Center for Precision Medicine under [www.bcpm.unibe.ch](http://www.bcpm.unibe.ch)