UNIVERSITÄT BERN

Faculty of Medicine

Department for BioMedical Research

Johanna Dürmüller-Bol DBMR Research Award 2026

The Johanna Dürmüller-Bol DBMR Research Award is a joint project of the Department for BioMedical Research DBMR and the Foundation Johanna Dürmüller-Bol. The award is intended to promote a younger researcher of the Faculty of Medicine, by supporting a promising research project with the aim of obtaining further funding through competitively acquired third-party funds.

Johanna Dürmüller-Bol DBMR Research Award 2026

At DBMR Day for BioMedical Research on July 1 2026, Prof. Mark A. Rubin announced the co-awardees of the Johanna Dürmüller-Bol DBMR Research Award 2026.

This year's award is shared equally between:

Dr. Elham Kashani

Institute of Tissue Medicine and Pathology, University of Bern

Dr. Christina Grimm

Department for BioMedical Research, University of Bern

For the project:

Beyond TGFβ: autocrine activin signaling as the cell-intrinsic engine of glioblastoma stem cell maintenance

For the project:

From building blocks to building interactions: decoding placental and maternal contributions to early gestation fetal brain development

The DBMR congratulates Dr. Kashani and Dr. Grimm and thanks the Foundation Johanna Dürmüller-Bol for their continuing support!

Beyond TGFβ: autocrine activin signaling as the cell-intrinsic engine of glioblastoma stem cell maintenance

Dr. Elham Kashani

Lay Summary:

Glioblastoma is the most common and most aggressive primary brain tumor in adults and remains associated with an extremely poor prognosis. Over the past 15 years, therapeutic advances have been minimal, and emerging strategies such as targeted therapies and immunotherapies have failed to significantly improve patient outcomes. These limitations underscore a critical gap in our understanding of the biological mechanisms driving therapy resistance and tumor recurrence.

The aim of this work is to define the cell-intrinsic mechanisms that maintain the therapy-resistant, stem-like state in recurrent glioblastoma, to identify new targets for patients in whom temozolomide (TMZ) chemotherapy has failed.

Recurrence is known to be driven by a subpopulation of glioblastoma stem cells (GSCs) that survive treatment and re-initiate tumor growth. Based on my preliminary findings, TMZ-resistant GSCs secrete elevated levels of activins (*INHBA* and *INHBB*) and overexpress the activin receptor *ALK7*. Interestingly, this autocrine activin signaling maintains a SOX2/OCT4-positive stem-like cellular state in the GSCs. Conversely, silencing activin reverses stemness and restores TMZ sensitivity. Strikingly, all three branches of the TGFβ superfamily (TGFβ, Nodal, and Activin) converge on a self-amplifying loop of activin induction. A recent study established that TGFβ secretion is niche-dependent, creating spatially distinct TGFβ gradients within the tumor. I therefore hypothesize that, while the TGFβ-rich fibrotic niche initiates the dormant stem-like state at recurrence, an autocrine activin circuit sustains this state intrinsically, independently of continued niche signals, and acts as a self-reinforcing driver of TMZ resistance and recurrence.

To test this, I will combine spatial analysis of human glioblastoma tumors with a causal *in vivo* experiment. First, using a cohort of matched primary and recurrent glioblastoma FFPE tissues, I will generate the first spatially resolved map of the activin-stemness niche by multiplex immunofluorescence (MACSima) and high-resolution spatial transcriptomics (Visium HD), defining where activin-driven stem-like niches are located, how they relate to fibrotic TGFβ -rich regions, and which ligand (activin A or B) predominates at recurrence. Second, in orthotopic patient-derived xenograft models, I will test whether knockdown of activin ligands dissolves these stem-like niches and restores sensitivity to TMZ, using spatial transcriptomics at endpoint to read out niche architecture.

In summary, the objective of this research is to establish whether autocrine activin signaling is the cell-intrinsic engine that sustains glioblastoma stemness and TMZ resistance, and therefore whether blocking activin represents an innovative strategy to prevent recurrence in patients for whom effective treatment options are currently lacking. The spatially resolved, causally-validated dataset generated here will provide the foundation for a subsequent SNF Starting Grant developing activin-targeted therapy for the treatment-refractory recurrent glioblastoma tumors.

From building blocks to building interactions: decoding placental and maternal contributions to early gestation fetal brain development

Dr. Christina Grimm

Lay Summary:

Historically, scientists viewed the placenta simply as a passive tissue providing nutrients and oxygen to a growing fetus. Today, we know it actively shapes how the brain grows. This project investigates a specific time window during mid-pregnancy when a fetus transitions from being supported by the mother's uterus to relying completely on the placenta. More specifically, we aim to discover how the placenta communicates with the developing brain during this phase and how early brain development is affected when this placental support is impacted or fails.

When the placenta doesn't function properly it causes a condition called Intrauterine Growth Restriction (IUGR), in which the baby grows too slowly and doesn't reach its genetically determined growth potential. Clinically, babies affected by IUGR have a much higher risk of developing cognitive difficulties and learning disabilities later in life. It is still unknown exactly how these brain changes are triggered during pregnancy, making it impossible to predict or treat them early on. The project will use a mouse model to map out a time-sensitive **'placenta-brain support module'** that we propose operates at a mid-pregnancy transition via two major lines of communication: a hormonal and a cellular arm. While the hormonal arm will include comprehensive tracking of dynamic biochemical and hormonal signals that the placenta sends to stimulate brain growth, the cellular arm will focus on how maternal immune cells crossing the placenta and engrafting in fetal tissue helps setting up the fetal brain's immune system from an early age. By intentionally introducing low-oxygen environments, we aim to disentangle exactly how these two communication lines break down, and how that breakdown negatively impacts early stages of brain development.

Ultimately, our results will shed light on this underexplored but highly critical pregnancy window and will lay the groundwork for further research focusing on identifying maternal and/or placental biomarkers that can predict if a baby's brain development is at risk. This would open the door for timed, personalized treatments during pregnancy or right after birth to protect the child's long-term brain health.