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Faculty of Medicine

Department for BioMedical Research

Johanna Dürmüller-Bol DBMR Research Award 2025

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.

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At DBMR Day for BioMedical Research on July 2 2025, Prof. Mark A. Rubin announced the awardee of the Johanna Dürmüller-Bol DBMR Research Award 2025.

The award went to:

Dr. Benedetta Coppe

Institute of Anatomy, University of Bern

For the project:

Impact of Cardiac Injury on Male Reproductive System and Gametes Chromatin Accessibility

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

Lay Summary:

While experiences lived by one generation are usually not transmitted to the following, some exceptions to the rule have been reported. In fact, in response to specific ancestral stressors, such as exposure to toxicants or unhealthy diets, it has been observed that the offspring of exposed individuals might develop altered phenotypes. Interestingly, DNA methylation and histone post-translational modifications, two epigenetic marks affecting chromatin conformation, have been found perturbed in the gametes of exposed parents, possibly regulating the transmission of altered information from one generation to the next [1].

In mice, we were able to prove that a paternal heart injury influences heart development and the damage response of the next generation [2]. These results have aroused great interest [3-4]. Consistent with our results in animal models, human data showed that pre-existing parental cardiovascular disease (CVD) increases offspring's risk of developing CVD early in life [5].

Yet, the mechanisms by which cardiac injury affects the reproductive system, altering the information transmitted from one generation to the next, remain unknown.

Thus, this project aims to elucidate how neonatal cardiac damage affects gonads and gametes in mice.

In adult mice, systemic inflammation is observed in multiple organs in response to cardiac injury, with some showing long-lasting alterations [6]. Thus, it is plausible that the reproductive system is similarly affected, either developing acute or chronic inflammation.

To understand whether and how systemic inflammation affects the gonads following neonatal cardiac damage, inflammatory signs will be assessed early after cardiac injury and later in life using transcriptomics and immunostaining approaches. One hypothesis is that, early in life, acute inflammation affects the reproductive system, inducing persistent changes in the already developed spermatogonia. Alternatively, a persistent inflammatory state in the reproductive system of adult mice originating from unresolved cardiac healing [7] could influence the information carried by gametes undergoing spermatogenesis.

Chromatin accessibility changes and their regulation through putative transcription factors will be additionally addressed at the single-cell level in adult animals. Data from single-nuclei ATAC-seq performed on the gonads of adult mice will identify chromatin regions with altered accessibility and predict transcription factors that may regulate these loci following neonatal cardiac injury. These data will lay the groundwork for future studies on the epigenetic changes triggered by early-life cardiac damage and will provide a list of potential therapeutic targets to block the transmission of altered information to the next generation.

Finally, if future studies confirm shared molecular and epigenetic mechanisms between mice and humans, data obtained within the framework of this project will help define the critical intervention time to impede or reverse the establishment of modification in gametes and prevent the transmission of altered information through generations.

Only in Switzerland, around 120 children born with congenital heart disease undergo heart surgery within the first six weeks of life [8]. Therefore, investigating how neonatal cardiac damage influences gonads and gametes is paramount to identifying targetable pathways that may prevent the intergenerational transmission of altered information.

[1] *Fitz-James M. H. and Cavalli G., 2022, Nature Research. doi: 10.1038/s41576-021-00438-5.*

[2] *Coppe B. et al., 2025, Circulation 151(13):968–71. doi:10.1161/CIRCULATIONAHA.124.070323*

[3] Koehler, X., 2025, *Nat Cardiovasc Res* **4**, 497 (2025). https://doi.org/10.1038/s44161-025-00663-9 **[4]** Dr. Lutz und Dr. Celia Zwillenberg-Preis 2024

[5] *Hossin M. et al., 2024, European Heart Journal 45(38). doi:10.1093/EURHEARTJ/EHAE547.*

[6] *E. Cortada et al., 2024, Communications Biology, doi: 10.1038/s42003-024-07315-x*

[7] *Lam N. T. and Sadek H. A., 2018, Circulation, doi: 10.1161/CIRCULATIONAHA.118.033648*

[8] *Natterer J. et al., 2022, Swiss Med Wkly, doi: 10.4414/SMW.2022.W30217*