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Ph.D. and Postdoctoral Positions on Translational Quality Control: Mechanisms, Role in Neurodegeneration, and Drug Discovery

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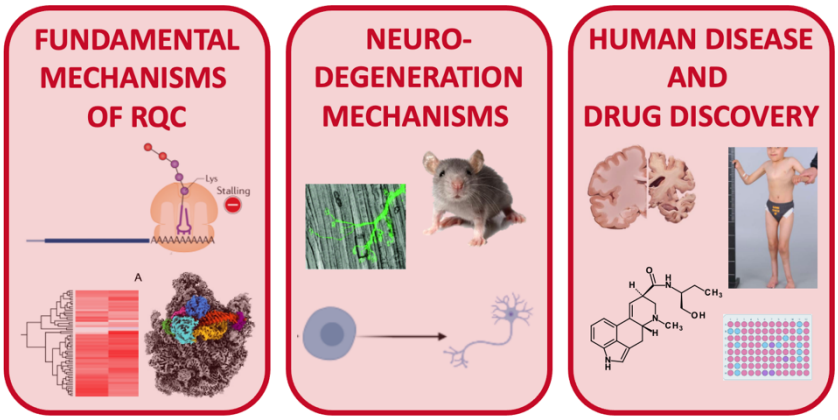
September 2022: Ph.D. and Postdoctoral positions are available in the Joazeiro laboratory at the Center for Molecular Biology of Heidelberg University (ZMBH), Germany.

A general interest of the lab is to investigate the function of E3 ubiquitin ligases in biology and disease. We also take advantage of our E3 ligase expertise to develop small-molecule protein degraders, or PROTACs, a new modality of molecular therapeutics (to know more, see www.joazeirolab.com).

For the past decade, we have devoted much focus towards studying a protein quality control pathway we discovered, now known as Ribosome-associated Quality Control (RQC) (Bengtson & Joazeiro 2010. ***Nature*** 467:470). In RQC, the Listerin/Ltn1 E3 ligase mediates the proteolytic targeting of incomplete polypeptides produced when ribosomes stall during translation (Filbeck et al 2022. ***Mol Cell*** 82:1451).



Our research team undertakes different approaches to study fundamental RQC mechanisms, including biochemistry, structural biology, and mammalian tissue culture (e.g., Thrun et al 2021. ***Mol Cell*** 81:2112; Filbeck et al 2021. ***Mol Cell*** 81:104).

Importantly, we have found that mutations that impair RQC cause ALS-like neurodegenerative phenotypes in mice (Chu et al. 2009. ***PNAS*** 106:2097; Martin et al. 2020. ***Nature Comm*** 11:4625) so we also investigate the molecular mechanisms of neurodegeneration caused by RQC defects. Among other approaches, we utilize human iPSCs with CRISPR-engineered RQC mutations to generate i-motor neurons for analyses in tissue culture, either alone or as organoids.

Finally, we have recently made the landmark discovery that RQC also exists in bacteria (Lytvynenko et al 2019. ***Cell*** 178:76; Cerullo et al 2022. ***Nature*** 603:509). Whereas Listerin—like the ubiquitin system in general—is absent in prokaryotes, the Listerin co-factor Rqc2/NEMF has homologs in bacteria and archaea. We have found that bacterial Rqc2 itself is able to target aberrant nascent chains for degradation, by marking nascent chains with C-terminal alanine tails that function as degrons directly recognized by proteases! By studying related processes in diverse organisms we expect to acquire insights and, ultimately, deeper understanding of the logic of the system and its evolution.

Positions are available to study any of the above topics. The candidate should have strong background in biochemistry and molecular genetics. Please see additional application information in our website, www.joazeirolab.com