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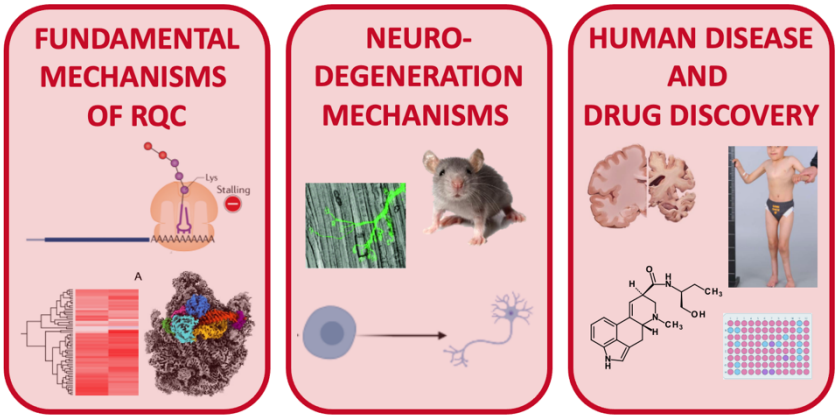
European Research Council

ERC-funded Ph.D. Positions on
Translational Quality Control:
Mechanisms and Role in Neurodegeneration

July 2025: Ph.D. positions funded by the **European Reseach Council (ERC)** are available in the Joazeiro laboratory at the Center for Molecular Biology of Heidelberg University (ZMBH), Germany.

Our lab discovered a key protein quality control mechanism now known as Ribosome-associated Quality Control (RQC) (Bengtson & Joazeiro 2010. ***Nature*** 467:470). In this pathway, the Listerin/Ltn1 E3 ubiquitin ligase promotes the degradation of incomplete polypeptides produced when ribosomes stall during translation.



Over the past decade, we have focused on elucidating molecular mechanisms of RQC (for a review, see Filbeck et al 2022. ***Mol Cell*** 82:1451). Notably, we recently made the landmark discovery that an ancestral form of RQC also exists in bacteria, mediated by RqcH, a homolog of the Listerin co-factor, Rqc2/NEMF (Lytvynenko et al 2019. ***Cell*** 178:76; Cerullo et al 2022. ***Nature*** 603:509). Given the absence of Listerin—and the ubiquitin system in general—in bacteria, RqcH itself targets aberrant nascent chains for degradation. It marks the nascent chains with C-terminal alanine tails, which act as degrons recognized by proteases! Remarkably, this pathway is highly conserved: the Rqc2/RqcH ortholog, NEMF, also modifies nascent chains with alanine tails. In humans, this modification is recognized by two other E3 ligases, in a Listerin-independent fashion (Thrun et al 2021. ***Mol Cell*** 81:2112). Thus, by studying related processes across species, we are gaining insights into their molecular logic and evolution.

Importantly, we have shown that mutations impairing RQC cause ALS-like neurodegenerative phenotypes in mice and humans (e.g., Martin et al. 2020. ***Nature Comm*** 11:4625). We are therefore also investigating the molecular mechanisms of neurodegeneration caused by RQC defects and the role of RQC in human neurodegenerative disease. Our approaches include using CRISPR-engineered human iPSCs with RQC mutations to generate i-neurons for biochemical and imaging studies.

Our team employs a wide range of experimental systems and techniques, including biochemistry, molecular genetics, structural biology (in collaboration with the cryo-EM lab of Stefan Pfeffer), mammalian tissue culture, and diverse model organisms—from bacteria to mice (e.g., Thrun et al 2021. ***Mol Cell*** 81:2112; Filbeck et al 2021. ***Mol Cell*** 81:104).

Positions are available to work on any of the above research topics. Ideal candidates will have a strong theoretical background in biochemistry and molecular genetics. Please see additional application information in our website, **www.joazeirolab.com**