



Joint Projects

1. Investigating the Role of ER Proteostasis and Lipid Signaling in Epithelial Stem Cell Plasticity and Skin Homeostasis 2
2. Mitigating *N*-Nitrosamine Formation in Drugs with Vulnerable Amines by Co-Crystallization with Nitrite Scavengers and Antioxidants 4



1. Investigating the Role of ER Proteostasis and Lipid Signaling in Epithelial Stem Cell Plasticity and Skin Homeostasis

Date Posted	13 February 2026	
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Partner University	University of Turin	
Supervisors	Home	Partner
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Project Description (200-300 words)	<p>The maintenance of epithelial tissues depends on the remarkable plasticity of stem cells, which must navigate complex proteostatic and metabolic shifts during wound healing and tissue regeneration. At the core of these adaptive responses is an ER stress-responsive transcription factor network downstream of sensors such as the Unfolded Protein Response (UPR), which reprograms gene expression to restore proteostasis or drive cell fate transitions. The endoplasmic reticulum (ER) serves as a central hub for protein quality control (PQC) and lipid biosynthesis, both of which are critical for maintaining cellular identity and responding to environmental stress. However, the mechanisms by which ER stress-induced transcriptional programs and lipid signaling pathways coordinate epithelial stem cell dynamics remain poorly understood.</p> <p>This collaborative project between Guillaume Thibault (Nanyang Technological University) and Giacomo Donati (University of Turin) aims to dissect how the ER-mediated stress response, its underlying transcription factor network, and lipid homeostasis govern skin stem cell plasticity and homeostasis. Leveraging preliminary data, single-cell RNA sequencing (scRNA-seq), and chromatin/transcriptional profiling, we will investigate how disruptions in ER proteostasis reshape gene regulatory programs to influence the transition of epithelial cells into regenerative or oncogenic states.</p> <p>Specifically, the project will (1) define the ER stress-responsive transcription factor network and identify key PQC factors and ER stress sensors activated during epithelial wound healing and lineage commitment; (2) utilize lipidomics and lipid-flippase analysis to determine how changes in membrane composition, regulated by proteins like CLPTM1L, influence stem cell signaling and stress-induced transcriptional reprogramming; (3) develop engineered skin models to test how modulating ER proteostasis and associated</p>	



	<p>chromatin states can enhance tissue repair or inhibit stress-induced tumorigenesis.</p> <p>By combining expertise in ER biology and lipidomics from from the Thibault lab with Donati Lab's mastery of epithelial stem cell dynamics, in vivo skin models, and chromatin/transcriptional regulation, this project will provide novel insights into the fundamental mechanisms of tissue health and disease.</p>
Program/Center Website(s)	NA
Additional Information (e.g., files with project details)	NA



2. Mitigating *N*-Nitrosamine Formation in Drugs with Vulnerable Amines by Co-Crystallization with Nitrite Scavengers and Antioxidants

Date Posted	10 December 2025	
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Partner University	University of Turin	
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Project Description (200-300 words)	<p>A widely prescribed drug, ranitidine hydrochloride, was globally recalled in 2019 due to concerns over the presence of a probable human carcinogen <i>N</i>-Nitrosamine (NS) impurities. Contaminations of other drug substances (e.g., valsartan, metformin, nizatidine) with NS impurities have also been reported. NS impurities are formed by reactions between vulnerable amines of the drug substance (DS) and nitrosating agents, which typically originate from nitrite impurities present in the raw materials used in DS/drug product (DP) production (e.g., solvents, excipients).</p> <p>Current mitigation strategies for NS formation rely on adding nitrite scavengers and/or antioxidants in the tableting step. The current strategy's effectiveness hinges on NS inhibitors being always available in the vicinity of the DS and at high enough concentration, which is certainly not a given. To overcome this limitation, this project aims to incorporate the NS inhibitors into the drug crystals themselves via their co-crystallization. This approach ensures co-existence of the NS inhibitors and drug substance at the molecular level.</p> <p>Molecular structure-based screening of various NS inhibitors in terms of their co-crystallization propensity with the model drug will first be carried out. Co-crystals of the promising NS inhibitors will be prepared by either liquid-assisted grinding or solvent evaporation. The co-crystals will be incorporated into DP after which their NS inhibition effectiveness will be evaluated.</p>	
Program/Center Website(s)	NA	
Additional Information (e.g., files with project details)	NA	