

Internship offer Master 2 Franco-Croate

Host lab	INEM UMR7355
Team	Immunology
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Title: Skin epithelium damage activates the cGAS/STING pathway	
Summary Background: We showed before that a complex formed by the CXCL10 chemokine and commensal skin microbial DNA activates type I IFN responses facilitating skin damage repair (Di Dominizio et al 2020). Our laboratory reported that free DNA is released in the lung upon particle exposure and activates the DNA sensing pathway cGAS/STING and is crucial for silicosis and other respiratory pathologies (Benmerzoug et al 2018, 2019). Hypothesis: Host derived DNA released upon epithelial mechanical damage activating the DNA sensing cGAS-STING- type I IFN pathway contributes to wound repair. Approach: Investigate the gene and protein expression of cGAS-STING following injury of human keratinocytes and of mouse ear skin as well as the wound repair. Experimental models: A. Scratch injury of human skin monolayer culture induced repair will be followed in culture with analyses for cGAS-STING- type I IFN mRNA and protein. B. Tape strip injury (TSI) inflammation induced cGAS-STING- type I IFN expression in the skin analysed over 5 days. The role of cGAS-STING for the inflammatory and repair response will be tested in cGAS-STING deficient mice and compared with controls. The models are established in the laboratory at INEM and an engineer will assist. Key measurements: Detection of self DNA by picogreen assay and rtPCR. Activation of cGAS-STING gene and protein expression by rtPCR and Western blot. Microscopic analyses of injured keratinocytes and of TSI on the skin. Test the repair response in cGAS-STING deficient and litter-mate control mice. Expected results: cGAS-STING are activated and contribute to the inflammatory and repair response. Di Dominizio J et al Nat Immunol. 2020 Sep;21(9):1034-1045. doi: 10.1038/s41590-020-0721-6. Benmerzoug S et al Trends Immunol. 2019 Aug;40(8):719-734. doi: 10.1016/j.it.2019.06.001.	

Références et financements (5 publications relatives au sujet)

Di Dominizio J et al Nat Immunol. 2020 Sep;21(9):1034-1045. doi: 10.1038/s41590-020-0721-6.

Benmerzoug S et al Trends Immunol. 2019 Aug;40(8):719-734. doi: 10.1016/j.it.2019.06.001.

Benmerzoug S et al Nat Commun. 2018 Dec 6;9(1):5226. doi: 10.1038/s41467-018-07425-1.

Jiang Z et al J Invest Dermatol. 2017 Dec;137(12):2620-2629. doi: 10.1016/j.jid.2017.07.820.

Li, C et al J Invest Dermatol. 2017 Dec;137(12):2620-2629. doi: 10.1016/j.jid.2017.07.820.

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