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Cell surveillance of the mechanical integrity of the apical ECM

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If applicable, name of co-supervisor 2:

Abstract (10 lines)

Epithelia are in constant interaction with adjacent extracellular matrices (ECMs), which area source of biochemical signals and provide mechanical support. While the role of basal ECMs in relaying mechanical information to influence cell migration or fate has been well described, less is known about apical ECMs (aECMs) in animals. In *C. elegans*, mechanical coupling of the aECM to the epidermis is important during elongation in embryos (1). We have shown that in adults, mutant with structural changes that soften the aECM activate an immune response similar to physical injury or infection (2). We propose to explore the biophysical properties of the skin, by measuring the visco-elastic properties of the aECM in wild-type and different mutants, as well as to define the mechanical threshold required to trigger the immune response. These will be key to decipher how a cell can surveil the mechanical integrity of the apical ECM.

Keywords

aECM, tension, visco-elastic properties, mechanosensitivity, atomic force microscopy (AFM), laser nanoablation, innate responses, *C. elegans*

Objectives (5 lines)

To assess the biophysical properties of skin, we will compare and combine viscoelastic properties obtain with AFM and nanoindenter upon different mechanical load, and aECM elasticity measure with aECM nanoablation, in collaboration with Chardes Claire IBDM (4), in the wild-type and different relevant mutants. Performing AFM and nanoablation measurements in parallel will allow a direct comparison of contact mechanics and tension relaxation models on the same system. By developing a coupling of these 2 set-ups with fluorescence microscopy, we will then define the mechanical threshold that triggers calcium and cytoskeleton responses in the epidermis (3).

Expected profile (5 lines)

A student with a background in soft-matter physics is required to conduct the project. Experience with all steps of sophisticated imaging techniques (sample preparation, data acquisition and processing) and an interest in biology, particularlymodel animals, would be an advantage, as would knowledge of quantitative modeling approaches.

Is this project the continuation of an existing project or an entirely new one?
In the case of an existing project, please explain the links between the two projects (5 lines)

This is a new collaboration between Centuri members that relies on the expertise in AFM and nano-ablation. It builds on a project in which Partner 1 identified, through genetics and cell biology, a potential mechanotransduction pathway linking aECM integrity to the immune response. It is key to provide insight into the physical nature of this mechanosensory connection which would then be model in collaboration with a theoretical physicist R. Voiturier and M. Labouesse at the IBPS.

2 to 5 references related to the project

1- Vuong-Brender, T.T., Ben Amar, M., Pontabry, J., and Labouesse, M. (2017). The interplay of stiffness and force anisotropies drives embryo elongation. Elife 6. 10.7554/eLife.23866.

2- Aggad, D., Brouilly, N., Essmann, C.L., Richard, F., Omi, S., Cazevieille, C., Hall, D.H., Ewbank, J.J., Pujol, R., and Pujol, N. (2021). Meisosomes, folded membrane platforms, link the epidermis to the cuticle in *C. elegans*. BioRxiv https://tinyurl.com/9yty6dt3.

3- Taffoni, C., Omi, S., Huber, C., Mailfert, S., Fallet, M., Rupprecht, J.F., Ewbank, J.J., and Pujol, N. (2020). Microtubule plus-end dynamics link wound repair to the innate immune response. Elife 9, e45047, e45047. 10.7554/eLife.45047.

4- Bambardekar, K., Clement, R., Blanc, O., Chardes, C., and Lenne, P.F. (2015). Direct laser manipulation reveals the mechanics of cell contacts in vivo. **PNAS**. 112, 1416-1421. 10.1073/pnas.1418732112.

3 main publications from each PI over the last 5 years

Nathalie Pujol

Aggad, D., Brouilly, N., Essmann, C.L., Richard, F., Omi, S., Cazevieille, C., Hall, D.H., Ewbank, J.J., Pujol, R., and Pujol, N. (2021). Meisosomes, folded membrane platforms, link the epidermis to the cuticle in *C. elegans*. **BioRxiv** https://tinyurl.com/9yty6dt3.

Taffoni, C., Omi, S., Huber, C., Mailfert, S., Fallet, M., Rupprecht, J.F., Ewbank, J.J., and Pujol, N. (2020). Microtubule plus-end dynamics link wound repair to the innate immune response. **Elife** 9, e45047, e45047. 10.7554/eLife.45047.

Dodd, W., Tang, L., Lone, J.C., Wimberly, K., Wu, C.W., Consalvo, C., Wright, J.E., Pujol, N.*, and Choe, K.P.* (2018). A Damage Sensor Associated with the Cuticle Coordinates Three Core Environmental Stress Responses in *C. elegans*. **Genetics** 208, 1467-1482. 10.1534/genetics.118.300827.

Claire Valotteau

Valotteau, C., Sumbul, F., & Rico, F. (2019). High-speed force spectroscopy: microsecond force measurements using ultrashort cantilevers. **Biophysical reviews**, 11(5), 689-699.

Valotteau, C., Dumitru, A. C., Lecordier, L., Alsteens, D., Pays, E., Pérez-Morga, D., & Dufrêne, Y. F. (2020). Multiparametric Atomic Force Microscopy Identifies Multiple Structural and Physical Heterogeneities on the Surface of Trypanosoma brucei. **ACS. omega**, 5(33), 20953-20959.

Valotteau, C., Prystopiuk, V., Pietrocola, G., Rindi, S., Peterle, D., De Filippis, V., ... & Dufrêne, Y. F. (2017). Single-cell and single-molecule analysis unravels the multifunctionality of the Staphylococcus aureus collagen-binding protein Cna. **ACS nano,** 11(2), 2160-2170.