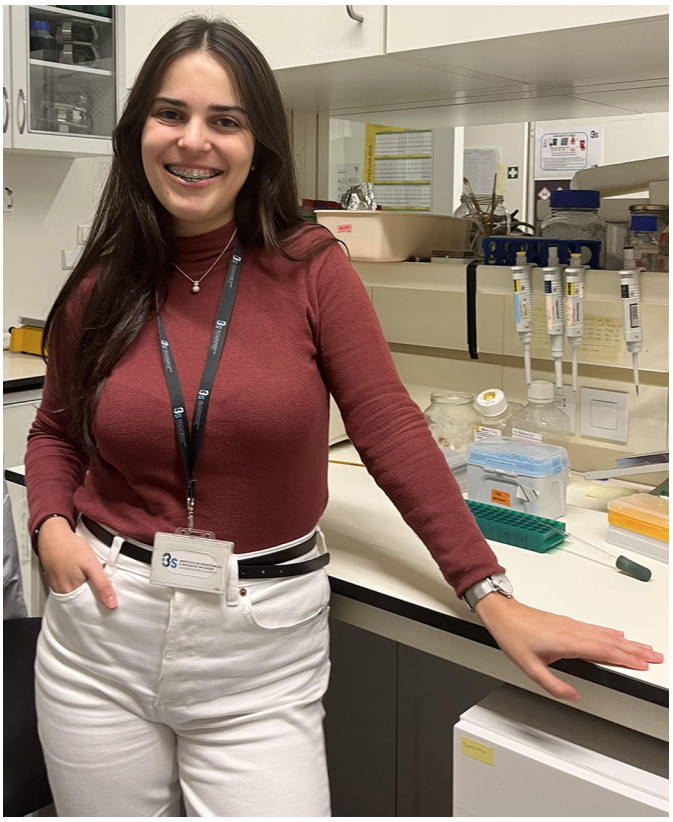
© 2023. Published by The Company of Biologists Ltd | Disease Models & Mechanisms (2023) 16, dmm050106. doi:10.1242/dmm.050106

FIRST PERSON

First person – Lídia Faria

First Person is a series of interviews with the first authors of a selection of papers published in Disease Models & Mechanisms, helping researchers promote themselves alongside their papers. Lídia Faria is first author on 'Activation of an actin signalling pathway in pre-malignant mammary epithelial cells by P-cadherin is essential for transformation', published in DMM. Lídia is a PhD student in the lab of Florence Janody at Universidade do Porto, Porto, Portugal, investigating how pre-malignant cells acquire characteristics of tumour cells.



Lídia Faria

How would you explain the main findings of your paper to non-scientific family and friends?

While some benign tumours, which are characterized by the presence of a non-cancerous mass of cells, never progress into malignant tumours and don't need to be treated, others may do so and grow and spread to other parts of the body. However, since medical doctors are still unable to predict whether non-cancerous tumours will or will not develop into a cancerous disease, all women diagnosed with a non-cancerous breast tumour are given unpleasant pharmacological treatment. Therefore, it is imperative to develop new approaches to distinguish between women with clear gain from therapy and women who will undergo unneeded and hazardous procedures.

To reach this goal, we have generated a fly avatar that carries the human gene that encodes for P-cadherin, as this molecule is present in high quantity in non-cancerous and breast tumour cells, which allowed us to identify MRTF-A and SRF, two key molecules that are activated by P-cadherin and are responsible for non-cancerous cells shift to cancer cells. We then used a human breast cell line, which recapitulates cancer development over time from 'normal' to non-cancerous and then to breast cancer, that validated our findings predicted by the fly avatar.

"[…] activation of the actin–MRTF-A–SRF signalling pathway by P-cadherin is required to promote malignant transformation, which opens the possibility to using this axis to predict which non-cancerous breast tumours will evolve to breast cancer."

What are the potential implications of these results for your field of research?

Our findings show that the activation of the actin–MRTF-A–SRF signalling pathway by P-cadherin is required to promote malignant transformation, which opens the possibility to using this axis to predict which non-cancerous breast tumours will evolve to breast cancer. This allows the selection of women with a non-cancerous breast tumour that will never evolve into breast cancer, so that they do not have to receive unnecessary painful pharmacological treatment.

What are the main advantages and drawbacks of the experimental system you have used as it relates to the disease you are investigating?

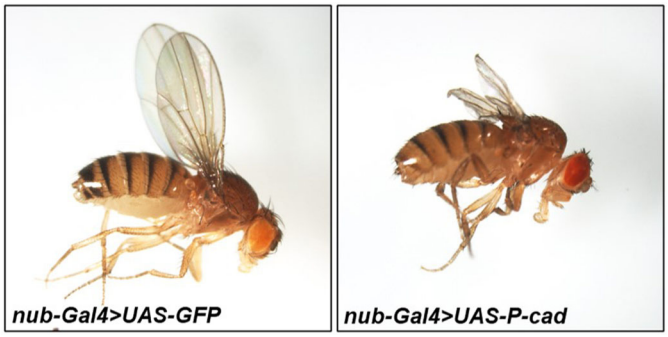
We have generated a new *Drosophila in vivo* model that mirrors the human breast carcinomas that express the cell adhesion molecule P-cadherin, which is highly enriched in basal-like breast carcinomas and has been implicated in all steps of tumour progression. This model, inducible with the Gal4-UAS system, presents a new clinically relevant platform to study P-cadherin effectors *in vivo*. We have also validated the findings we obtained using the *Drosophila* avatar in a human mammary epithelial cell line (MCF10A-ER-Src) that recapitulates malignant transformation upon activation of the *SRC* oncogene, which allows us to follow the multistep development of basal-like breast cancer.

What has surprised you the most while conducting your research?

Drosophila offers many advantages as an animal model to study the development of diseases given its large arsenal of genetic tools and rapid generation time. However, it does not express P-cadherin, our

Lídia Faria's contact details: i3S, Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Rua Alfredo Allen, 208, 4200-135 Porto, Portugal.
E-mail: lfaria@ipatimup.pt

Disease Models & Mechanisms (2023) 16, dmm050106. doi:10.1242/dmm.050106



Expressing the human P-cadherin gene in *Drosophila* under the control of the Gal4-UAS system leads to deficient development of the wings (right) compared to a fly that does not express P-cadherin (left).

protein of interest in this work, so we decided to generate a humanized fly that expresses this protein, and it was really exciting to see that we were able to recapitulate what happens in the human context.

What do you think is the most significant challenge impacting your research at this time and how will this be addressed over the next 10 years?

How can we improve the lives of patients that have been diagnosed with a non-cancerous lesion? For me this is a very important question in the field of cancer research. If we are able to protect some patients from experiencing the unpleasant side effects of pharmacological treatments because they have been identified with a non-cancerous lesion that is not problematic and probably will never acquire malignant characteristics, we will greatly enhance their quality of life! I believe that researchers today are cooperating to make patients' lives better so that in 10 years from now we are closer to this goal.

What changes do you think could improve the professional lives of scientists?

For me, it is really important to have the support of a good mentor/supervisor, as well as a good research team. Moreover, every researcher suffers from the pressure of publishing as high as possible, in terms of impact factor, as it is positively associated with higher opportunity of being awarded with a grant and receiving funding to follow research. For this reason, I truly believe that if we improve in these terms we improve our careers.

What's next for you?

I have just started my PhD, in which I want to keep understanding how what happens at the pre-malignant stage influences the transition to a malignant state. More precisely, I'm curious to know how malignant progression is modulated by the forces that cells withstand in their adherens junctions.

Reference

Faria, L., Canato, S., Jesus, T. T., Gonçalves, M., Guerreiro, P. S., Lopes, C. S., Meireles, I., Morais-de-Sá, E., Paredes, J. and Janody, F. (2023). Activation of an actin signaling pathway in pre-malignant mammary epithelial cells by P-cadherin is essential for transformation. *Dis. Model. Mech.* **16**, dmm049652. doi:10.1242/dmm.049652