3R Prize: human skin cultures to study psoriasis

This year's UNIGE 3R Prize honours work on psoriasis in which in vitro models of the human epidermis have replaced laboratory mice.

«Reduce», «Refine», «Replace»: based on these three principles, the 3R Prize of the University of Geneva (UNIGE) is awarded each year to a research project whose experimental model enabled a major scientific advance particularly respectful of the animal condition. This year's prize was awarded to a researcher from the Department of Medicine and from the Geneva Centre for Inflammation Research (GCIR), in the Faculty of Medicine. The jury rewarded a study in which the mouse models usually used to study psoriasis were completely replaced by in vitro cultures of human skin.

Created in 2016, the 3R Prize of the University of Geneva (UNIGE) recognises research projects that contribute to the advancement of knowledge in life sciences, while helping to «reduce», «refine» and «replace» (3R) the use of animal models. Awarded annually, the prize is worth CHF 5,000, which will be used to continue the work of the winning researchers. The 9th Prize was awarded on 4 June 2024 at the Faculty of Medicine Awards ceremony.

This year, the jury rewarded Maria Shutova, senior lecturer in the Department of Medicine and at the Geneva Centre for Inflammation Research in the UNIGE Faculty of Medicine, for her work on the molecular mechanisms in psoriasis, a chronic, auto-immune and inflammatory skin disease. The quality of life of psoriasis sufferers — between 3% and 7% of the population — is affected both by the manifestations of the disease, which cover the body in painful red patches, and by the side-effects of current treatments.

Entitled «Inflammation modulates intercellular adhesion and mechanotransduction in human epidermis via ROCK2» and published in iScience, this study deciphers the inflammatory mechanisms which, in psoriasis, deregulate the epidermal immune response.

Reconstructed epidermis is more faithful than animal models

Psoriasis research usually uses mouse models of the disease. However, the major biological differences between human and mouse skin mean that these models are imperfect. This is why Maria Shutova and her colleagues have been working to develop a more reliable experimental model. Using undifferentiated human skin cells and reconstructed human epidermis, they were able to faithfully reproduce the differentiation and stratification processes of human skin. The scientists then modelled the inflammation typical of psoriasis by stimulating their cultured cells with a cocktail of cytokines — small proteins involved in cell communication and immune reactions.

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Prof. Sébastien Castelltort, (Vice-Rector Research & Sustainability, UNIGE), Dre Maria Shutova (3R Prize 2024), Prof. Patrycja Nowak-Sliwinska, (President of the Jury, 3R Prize), at the award ceremony on 4 June 2024.

High resolution pictures

Deciphering cell communication problems

Using their model, the research team discovered that in psoriasis, epithelial cells are no longer able to detect and correctly interpret the stimuli they receive in order to translate them into appropriate electrochemical signals. Inflammatory cytokines then lead to the activation of a particular cellular communication pathway and an inflammatory response. An enzyme, ROCK2, appears to be involved. Scientists have now identified a small molecule capable of inhibiting this enzyme, KD025, opening up the hope of a new treatment.

These results, which are much more relevant to human pathology than those obtained with non-human models, validate a new experimental model. Entirely in vitro and widely applicable and reproducible for studying inflammatory phenomena in the skin, it advantageously replaces the use of animals in this context. «By using new technologies and sharing knowledge, Dr. Shutova has brilliantly integrated the 3Rs principle and is proposing a useful solution for other research laboratories», says Daniele Roppolo, Director of Animal Experimentation at the UNIGE.

UNIGE proactive in promoting the 3Rs

This year's 3R Prize jury was composed of five UNIGE researchers: Patrycja Nowak-Sliwinska (President of the 2024 jury and winner of the 2020 3R Prize), Pascal Senn (winner of the 2022 3R Prize), Thierry Soldati (winner of the 2019 3R Prize), Ivan Rodriguez and Martina Valentini. Six applications were submitted. «This shows that the major efforts made by the Animal Experimentation Department and the Rector's Office to promote the 3R are bearing fruit,» says Elsa Giobellina, UNIGE's Animal Protection Officer.

The UNIGE runs regular information campaigns to inform researchers about sources of funding, existing awards and training opportunities for 3R projects, both within and outside the university. It also organises 3R seminars and is a member of the Swiss 3R Competence Centre (3RCC), which promotes animal-friendly research at national level.

contact

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For award-winning research

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