Protein citrullination in cell physiology and disease.

https://www.neurodegenerationresearch.eu/survey/protein-citrullination-in-cell-physiology-and-disease/

Name of Fellow

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Institution
Funder

Wellcome Trust

Contact information of fellow
Country

United Kingdom

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Protein citrullination in cell physiology and disease.

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The project/programme is most relevant to:

Neurodegenerative disease in general

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alzheimer | MotorNeuron | Neurodegen

Research Abstract

The post-translational modification (PTM) of proteins is central to the regulation of most cell functions and provides an enormous degree of additional complexity to the proteome. The post-

translational conversion of peptidylarginine to citrulline (citrullination) is carried out by a small family of enzymes called peptidylarginine deiminases (PADIs). It is found on proteins of different functional categories and is therefore likely to regulate diverse cellular processes. Importantly, abnormal ci trullination is a feature of various pathological states including autoimmunity, neurodegeneration, atherosclerosis and cancer. It serves as a diagnostic and prognostic marker and its inhibition has shown efficacy in disease models. I recently showed that the nuclear deiminase PADI4 regulates pluripotency and identified a new molecular mechanism by which it mediates chromatin decondensation. Using high resolution proteomics I defined the citrullinome in cell types where PADI4 is functionally r elevant. I will extend this work to define the molecular causes of PADI4 activation and its consequences for pluripotency, self-renewal, DNA methylation and the development of acute myeloid leukaemia. This work will advance the current understanding of citrullination, help to delineate new modes of regulation of cell physiology and disease and may uncover knowledge that is of prognostic, diagnostic and therapeutic value.

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Fellowships

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