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Transthyretin internalization by sensory neurons is megalin mediated and necessary for its neuritogenic activity

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About the work

Mutated transthyretin (TTR) causes familial amyloid polyneuropathy, a neurodegenerative disorder characterized by TTR deposition in the peripheral nervous system (PNS). The origin/reason for TTR deposition in the nerve is unknown. Here we demonstrate that plasma TTR has access to the nerve. We previously determined that in the absence of TTR, both neurite growth in vitro and nerve regeneration in vivo were impaired. Reinforcing this finding, we now show that local TTR delivery to the crushed nerve rescues the regeneration phenotype of TTR knock-out (KO) mice. Moreover, we show that in vitro, in neurons, megalin receptor-mediated TTR internalization is needed for TTR regeneration-enhancer activity. In conclusion, our work unravels the mechanism of TTR action during nerve regeneration. Additionally, TTR presence in the nerve, as is here shown, may underlie its preferential deposition in the PNS of familial amyloid polyneuropathy patients.

About the author

Carolina Estima Fleming has obtained a degree in Aquatic Sciences at ICBAS in 2002. She then joined the BEB PhD Program at the University of Coimbra and developed her PhD research project at the Molecular Neurobiology group- IBMC, Porto. In 2008, Fleming CE obtained a PhD degree in Molecular Biology at the University of Coimbra. During that period, Carolina Fleming investigated the role of transthyretin in peripheral nerve biology. From her PhD research, Fleming CE published 3 papers (including a paper in Journal of Neuroscience), 1 book chapter and 3 reviews (including a review in Progress in Neurobiology). With part of this research, Fleming CE was awarded in 2006 the Pfizer Prize for Basic Research. Currently Fleming CE is an Invited Professor of Histology and Embryology at ICBAS and a Member of the Scientific Committee of the Master in Marine Science at the same institution.