

Highthroughput analysis of the conjugating enzymes (E2s) of ubiquitin and ubiquitin-like proteins

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We developed a pipeline for highthroughput homology modelling of the E2 enzymes followed by automated analysis of their physico-chemical properties. The E2s are a part of the pathway for conjugating ubiquitin family proteins to their target substrates and as such are important for many aspects of cell regulation, for example the cell cycle. Dysregulation of the ubiquitin system has been implicated in many diseases including cancer and neurodegeneration. Here we present issues arising from the modelling process as well as analysis of the sequence structure and function of the E2s. In particular we have discovered a putative E1 binding motif, and a relationship between various E2s and their electrostatic potentials, most notably with regard to SUMO conjugation and the ubiquitination of mitotic cyclins. We have also developed a website to present our data and other data relevant to ubiquitination (www.ubiquitin-resource.org). A long term goal is small molecule inhibition of these enzymes.