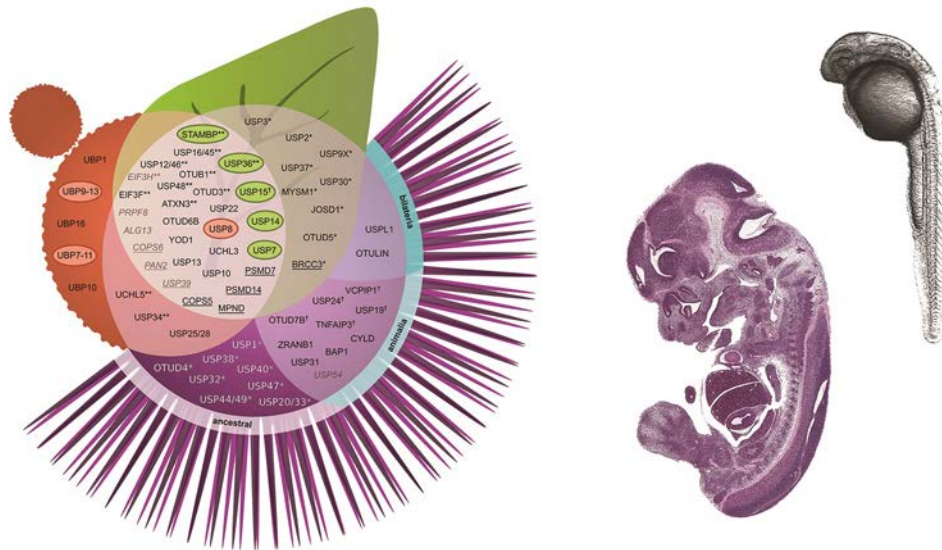




Origin and diversification of the deubiquitinating enzymes



Vertebrate genomes encode approximately one hundred deubiquitinating enzymes (DUBs) that collectively contribute to the proteostatic regulation of a much larger number of substrates. We have reported that the multiplicity of DUBs can be explained largely by gene duplication, and have speculated that subsequent subfunctionalization of DUBs has contributed to substrate specificity. This leaves us with a conundrum: how can new enzyme/substrate relationships evolve without disruption of existing (and in many cases essential) pathways? We are exploring this problem by studying USP4 and USP15, two ohnologs implicated in a number of diseases including cancer. USP4 and USP15 have acquired unique substrates in Wnt, TGF- β , DNA repair, innate immunity, and cell fate pathways. An understanding of their functional divergence may inform targeted therapies.

Dr. Doug Gray

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Host: Dr. Lori Frappier

Date: Thursday, December 13, 2018

Time: 10:00 AM

Place: MSB 3278