

The mystery of ABCB1 / ABCB4 gene evolution in birds

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The family of ABC transport proteins is widely expressed across a range of tissues and organs, observed in a multitude of species. Despite their structural similarities, they facilitate the transmembrane transport of a diverse range of substrates. ABCB1 (syn. MDR1 or P-glycoprotein) is expressed in a multitude of organs, particularly the small intestine, liver, kidney, and brain. It transports mainly xenobiotics. The same function is fulfilled by ABCB5; however, this carrier is specifically expressed in cancer cells, including malignant melanoma. In contrast, ABCB4 (syn. MDR3) is specifically located in the liver and catalyzes the export of phospholipids in the biliary tract.

Considering the structural similarities observed among these carriers, a gene duplication of ABCB1 is proposed as a potential origin for ABCB4 and ABCB5. To gain further insight into this matter, the related gene clusters were subjected to detailed phylogenetic analysis. A gene cluster is defined as a group of genes that occur in a specific order within the genome of different species. A change in this specific structure of the genome may be indicative of an evolutionary event. In the present project, we focused on different bird and reptile species and reported the existence of a highly conserved gene cluster for all the aforementioned genes. In mammals, ABCB1 and ABCB4 are considered as gene homologs. However, in birds, alternative and partly conflicting nomenclatures are provided in the NCBI and Ensemble databases. Genes with high homology to ABCB1 and/or ABCB4 are either designated as ABCB1-like / ABCB1LA, or ABCB4-like. In this case it is neither clear which of these bird and reptile genes phylogenetically and functionally resembles the human ABCB1 and ABCB4 genes, nor if these genes are homologs at all. Even more interesting, in some species belonging to the Neoaves clade, only one single ABCB1/ABCB4 gene homolog can be found with no clear preference for ABCB1 or ABCB4. Given the considerable distance between the bird/reptile and mammalian ABCB1/ABCB4 branches and the diverse nomenclature of the bird and reptile gene homologs, we propose to provisionally name these ABCB1-like / ABCB1LA and ABCB4-like genes as ABCB31 and ABCB32, until functional transport assays can experimentally prove functional homology to one of the human ABCB1 or ABCB4 genes.