Additional file 3  - PXR activation and bile salt pathways

All bile salts are derived from cholesterol, a 27-carbon molecule. The earliest bile salt pathway to evolve was to create bile alcohol sulfates with the 5α-orientation (A/B trans) [1, 2]. This pathway is used by the hagfish [3] and sea lamprey [4] (two examples from the superclass Agnatha), as well as African and Western clawed frogs (L.R. Hagey and M.D. Krasowski, unpublished data) and zebrafish [5]. The next pathway to evolve was likely 5β-bile alcohol sulfates, a route used in most cartilaginous fish (except Agnatha) but also found in some teleost fish, amphibians, and even a handful of mammals [1, 2, 6]. The evolutionarily most recent bile salt pathways are 24-carbon bile acids. These types of bile acids are produced by most mammals and birds, and some reptiles and teleost fish [1, 2, 6]. Primary bile acids are synthesized in the liver. Secondary bile acids are generated typically by intestinal bacterial enzymatic reactions on primary bile acids. (A) Human PXR is activated by both ‘early’ and ‘recent’ bile salts. Bile salts that activate human PXR are indicated in red. (B) Zebrafish PXR is activated only by ‘early’ bile salts. Bile salts that activate zebrafish PXR are indicated in red.

References:

