Chapter 4

The evolution of the retinol metabolism

Abstract

Introduction

The retinol metabolism comprises a series of enzymatic reactions that convert dietary vitamin A (retinol) into various bioactive compounds, primarily retinal for vision (REF) and retinoic acid for gene regulation (REF), ensuring the proper functioning of visual processes and other physiological roles in the body (REFS).

Retinol (Vitamin A1) is an essential micronutrient derived primarily from diet. It can be obtained directly from animal sources as retinyl esters or indirectly from plant sources as pro-vitamin A carotenoids, which are then converted into retinol in the body (REFS). Once in the cell, retinol is esterified to retinyl ester by the enzyme lecithin retinol acyltransferase (LRAT) (REF). When needed, retinyl ester is hydrolysed back to retinol (REF). Retinol is oxidized to retinal by retinol dehydrogenases (RDHs). Several other enzymes are involved in various steps of the retinol metabolism pathway as schematically shown in Figure 4.1 that summarizes what is known about the pathway according to the Kegg Pathway Database (REF). In addition, Table 4.1 provides a comprehensive list of these enzymes ranked by the number of pathways they participate in according to Kegg. Involvement in one or few pathways serves as an indicator of enzyme specificity to the retinol metabolism, as opposed to broad spectrum enzymes.

Retinal, particularly 11-cis-retinal, plays a crucial role in vision (REFS). 11-cis-retinal binds to the protein opsin in photoreceptor cells forming rhodopsin. Upon absorbing a photon, 11-cis-retinal is isomerized to all-trans-retinal, leading to a conformational change in opsin, and initiating a cascade of events called phototransduction (REFS) (see Chapter 3). After light exposure, all-trans-retinal is reduced to all-trans-retinol and then converted back to 11-cis-retinal through a series of enzymatic reactions. This part of the visual cycle is essential as it ensures the retina’s responsiveness to light (REFS). The regulation of the metabolic steps ensures sufficient 11-cis-retinal availability and prevents toxic build-up of intermediates. Additionally, retinal can be further oxidized to retinoic acid by retinaldehyde dehydrogenases (RALDHs). Retinoic acid serves as a signalling molecule that regulates gene expression and is critical for numerous developmental processes (REFS).

Given the importance of the retinol metabolism, it is compelling to delve into its evolutionary history, especially when considering the broader evolution of vision. Hence, the work presented in this chapter aimed to unravel this intricate history. The initial step was to identify the genetic components involved and determine their evolutionary relationships to answer questions such as: Do the gene families belong to overarching orthogroups? How closely related are they? The subsequent objective was to uncover the distribution of these components across the animal kingdom and, more broadly, within eukaryotes, to pinpoint the specific point in time when all the components came into place. The final endeavour was to delineate the main evolutionary events characterizing each orthogroup, to discern, for instance, if certain gene families have undergone a greater number of evolutionary events and contextualizing them within the evolutionary tree of life.

Results and Discussion

Enzymes involved in retinol metabolism belong to 12 major orthogroups.

Conclusions

Evolution:

Origins: The visual pigments, opsins, and the associated visual cycle have ancient origins. It's believed that the basic phototransduction machinery was present in the common ancestor of most extant animals.

Opsin Diversification: Over evolutionary time, different opsin classes evolved, allowing animals to detect light across different wavelengths. This diversification is tightly linked with changes in retinoid usage and the visual cycle.

Vertebrate Adaptations: The transition from aquatic to terrestrial environments necessitated changes in the visual system, including modifications in the retinoid pathway.

Retinoid Binding Proteins: Evolutionary changes in retinoid-binding proteins and enzymes have fine-tuned retinoid transport, storage, and metabolism, allowing diverse organisms to adapt to their specific visual environments.

Methods

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References