

Vitamin A and Retinoids

Japanese Society for Retinoids Research
November 21, 2008

Catharine Ross, Ph.D.
Pennsylvania State University



**PENN
STATE**

Past -- Vitamin A is now nearly 100 years old

Seminal discoveries--

Vitamin A “discovered” in 1913-15, by McCollum and Davis, Osborne and Mendel

Vitamin A deficiency, xerophthalmia, and impaired tissue/cell differentiation-- Mori, Wolbach and Howe, 1922-25

Vitamin A deficiency and infection -- Green and Mellanby, 1930

Retinol chemistry (synthesis and structure) -- Karrer* 1937, "for his investigations on carotenoids, flavins and vitamins A and B2"

Vitamin A as precursor of retinal; visual cycle -- Wald*, Hubbard and colleagues, 1950s "for ..discoveries concerning the primary physiological and chemical visual processes in the eye," 1967

Vitamin A status and the embryo-- Warkany, 1940s

Retinoic acid as active metabolite -- Arens and vanDorp, 1946; Dowling and Wald, 1960

More recent metabolic era--

Cellular vitamin A storage, morphology -- Ito, Wake and others, 1950s-present

Specific transport complexes in lymph, plasma and cells --Huang and Goodman, Muto and Goodman; Ong and Chytil, and then many others, 1960-70s-present

RA and embryonic patterning, Fell, Eichele, Tickle, 70s-present

Protein structure and function--Gordon, Li, Banasek, many investigators, 70s-present

Stellate cell biology-- Blomhoff, Norum, Senoo, 70s-present

Retinol metabolites--Roberts, DeLuca, Napoli and many others, 70s-present

Retinol metabolism-- many investigators, 70s-present

Transformative discoveries--

Nuclear retinoid receptors- 1987,
Chambon laboratory and Evans laboratory

Additional RARs, RAR β and RAR γ

RXRs

RAREs

Coactivators, corepressors, mediators

Future?

1) Challenges/great opportunities:

What do the 3 RARs, and 3 RXRs, do differently?

What genes and processes lie upstream of RA signaling during development?

(Shh, Fgfs, BMPs, RALDH, RARs, Gli, Tbx, etc--?)

2) Challenges/great opportunities:

A better understand of the regulation of genes that apparently do not respond through RAREs, but nonetheless are physiologically regulated by retinoids

A better understand the redundancy and complexity of endogenous retinoid production, and catabolism.

--Multiple substrates, multiple pathways, inducible & noninducible tissues

3) Challenges/great opportunities:

A better understanding of the applications of retinoids in tissue repair, stem cell research and regenerative medicine

How can we best harness the great power of retinoids as differentiation agents, in new ways, to improve the use of stem cells and enhance repair mechanisms?