



# CDB SEMINAR

## Akiko Maeda

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Wednesday, January 29, 2014

16:00~17:00 Auditorium C1F

## New therapies for retinal degenerative disorders

### Summary

Degenerative retinal diseases affect quality of life for over 50 million people worldwide, and there is a drastic lack of therapies available to patients. My research activity bridges between clinical and basic science application. In this seminar, paths for development of new pharmacologic therapies for ATP-binding cassette transporter (ABCA4)-associated retinal disorders will be discussed. The talk includes understanding of biology and biochemistry in vision, identification of therapeutic targets, validation of targets, assay development, creation of animal models, pre-clinical study, drug formulation for the retina, development of bio-imaging as well as introduction of modern pharmacological approaches including a systems pharmacology approach. Visual chromophore, 11-cis-retinal is regenerated through the visual retinoid cycle which is essential for vision. There are mainly two mechanisms for pathogenesis of retinal disorders associated with visual cycle impairments. One is the deficient supply of 11-cis-retinal, and the other is the build-up of byproducts after light perception. Our series of studies revealed that photo-activated visual chromophore, all-trans-retinal (atRAL) plays a central role for damaging the retina, even though this molecule is essential for regeneration of 11-cis-retinal for rhodopsin activation. ABCA4 is responsible for clearance of atRAL from photoreceptors together with all-trans-retinol dehydrogenase, RDH8. Combined deletions of ABCA4 and RDH8 in mice display retinal degeneration. ABCA4 abnormalities are found in patients with Stargardt disease, retinitis pigmentosa and age-related macular degeneration. Our pharmacologic approaches focus on controlled metabolism of atRAL and thereby reduced potential toxic atRAL-condensation products such as A2E. This seminar illustrates a strategy for the identification of new drug candidates and currently available drugs for the treatment of monogenic and complex diseases beyond the retina.

### Host:

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