2016 CARIG Conference Convenes in San Diego

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The Hilton Bayfront Hotel was the venue for the 2016 CARIG Conference, held on March 31, 2016, in association with the Experimental Biology meetings in San Diego, CA, USA. The overall conference theme was 'Carotenoids and Retinoids during Inflammation.' As usual, the proceedings began with the annual James Allen Olson *Perspectives in Carotenoids* Memorial Lecture; this year the lectureship went to Prof. Lewis P Rubin, MD of the El Paso Children's Hospital – Texas Tech University Health Sciences Center, El Paso, TX, USA. Prof. Rubin spoke on the topic of 'Vitamin A, Carotenoids and Inflammation in Infancy'. The full talk appears on p. 25–30 of this issue.

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This was followed by four presentations, each exploring specific facets of the mutual and bidirectional relationship between inflammation and infectious states and carotenoid status. Following the Olson Memorial Lecture, Prof. Sherry Tanumihardjo of the University of Wisconsin-Madison, Madison, WI, USA spoke on the keys to unlocking assessment of vitamin A status during inflammation. Inflammation causes changes in circulating acute-phase-response proteins. Some of these rise during inflammation – such as complement reactive protein, α_1-antitrypsin, and α_1-glycoprotein (positive acute-phase response) – whereas others – such as albumin, transferrin, retinol binding protein (RBP) and transthyretin (TTR) – decline in the circulation (negative acute-phase proteins). Important is that the latter two, RBP and TTR, are part of a complex that transports retinol in the blood. So inflammation reduces the carriage of vitamin A in the circulation and distorts the interpretation of serum retinol. Prof. Tanumihardjo pointed out that the modified retinol dose response test (one that involves dosing a subject with a vitamin A anolog, didehydroretinol) may be of special usefulness. In a state of true vitamin A depletion in the liver, stores of RBP have been accumulated above normal reserve levels. A spike release of vitamin A, detectable by monitoring the marker analog in the blood, provides a diagnostic approach to the nutrient's status, which is not distorted by inflammation or infection.

The second discourse in this series was given by Dr Torsten Bohn of the Luxembourg Institute of Health, Strassen, Luxembourg, who focused on anti-inflammatory aspects of carotenoids. Dr Bohn's discussion revolved around natural food sources of substances with anti-inflammatory activity. Under discussion were sources of polyphenols, such as plums and cabbages, and those yellow, orange and red fruits and vegetables that are known to be dietary sources of carotenoids. The leverage point seems to be the regulation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), with its suppression leading to anti-inflammatory outcomes. Citing *in vitro* experiments from his own laboratory, Dr Bohn asserted that carotenoids are more potent agents than polyphenolics because they have better transport characteristics in accessing the intracellular sites of NF-κB action. It is the polar cleavage products (apocarotenals) that are most important as NF-κB suppressors.

"Infections are known to deplete the body's vitamin A stores"

Next, Dr Charles Stephensen of the Western Human Nutrition Research Center, University of California, at Davis, CA, USA discussed carotenoid and retinol metabolism during infection and inflammation. Dr Stephensen focused on overt infection or on models of the activated acute reaction outlined a bidirectional relationship. He reiterated the theme of Dr Tanumihardjo – namely, that biomarkers of vitamin A status are distorted by inflammation, with circulating concentrations of retinol declining rapidly and profoundly. This is ascribed to redistribution from the bloodstream into central organs such as the liver. Infections are known to deplete the body's vitamin A stores. Diarrheal episodes predispose the body to poor absorption of non-breast-milk sources of vitamin A, while the vitamin A in maternal milk

Prof. Catharine Ross (left) and Prof. Sherry Tanumihardjo at the lectern during the 2016 CARIG conference in San Diego, CA, USA

remains well absorbed. Moreover, in inflammatory diarrhea and acute respiratory infections, vitamin A is excreted through the urinary tract due to the uncoupling of retinol from the RBP-TTR complex, which ordinarily serves to protect vitamin A from renal filtration.

The final contribution to the conference was by Prof. Catharine Ross of Pennsylvania State University, PA, USA, who was assigned the topic of acute inflammation effects on retinoid metabolism. Dr Ross conceded that inflammation can be a successful adaptive response in acute injury or invasion of an organism, but documented how the acute-phase response alters retinol transport, its cellular metabolism and the processes of immune function, dependent on the vitamin inducing inflammation. With injections of lipopolysaccharide (LPS) – a potent inflammatory agent – into rodents, the transcription leading to RBP synthesis is suppressed. LPS also downregulates the intestinal cleavage enzyme (BCO1), which releases active vitamin A from dietary provitamin A carotenoids. This impairs uptake of new vitamin A. The expression of retinoic acid-4-hydrolase (CYB26A1) is reduced by LPS. In terms of immune function, vitamin A status is important to the toll-like receptor (TLR) family of pattern-recognition receptors. Many aspects of immune defense are downregulated and suppressed in vitamin A deficiency, such as the containment and clearance of *Citrobacter freundii* in mice, who become asymptomatic carriers of the pathogen due to deficiency-induced Th17 B-cell dysfunction. Dr Ross's presentation, however, alluded to both acute and chronic inflammation, the latter of which occurs when the inflammation is unresolved and becomes chronic; this too is problematic. An interesting observation made by Dr Ross was that an amyloid response can only be mobilized in vitamin A sufficiency, such that vitamin A deficiency would be protective against amyloid accumulation.

The conference was followed in the evening by the VARIG-CARIG reception, in which three first-place prizes were awarded for excellence in graduate student and post-doctoral fellow research on carotenoids and vitamin A. The winners were Stephanie Mondloch of the University of Wisconsin-Madison, Madison, WI, USA; Emily Mohn of Tufts University, Boston, MA, USA; and Joshua Smith of the University of Illinois, Champaign, IL, USA.

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