



Carotenoid News

February 2015
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FROM THE EDITOR

*"Nothing great in the world has been accomplished
without passion."*

Hegel, German philosopher (1770-1831)

These words of Hegel must be remembered and taken to heart by all scientists, both young and old. Without passion, it is not likely that we may accomplish anything of importance in our research. CARIG events at the Experimental Biology meeting are notable for the infectious enthusiasm of carotenoid researchers, expressed in lively discussions of lectures and presentations, around posters and in social interactions. We invite you to study the agenda below and plan to attend them in Boston on March 27-29.

Maria S. Sapuntzakis (Chicago, IL)

CARIG Travel Awards

CARIG will award at least two monetary prizes, based on a poster competition to be held in conjunction with the CARIG Reception at Experimental Biology 2015 on Friday, March 27. Graduate students and postdoctoral trainees are eligible. Posters must address carotenoid and/or vitamin A research. For those assigned an oral presentation rather than a poster at EB'15, printed copies of your slides with a print copy of your abstract and a small banner may be used for the CARIG poster competition. No advance registration is required to participate in the poster competition. Contact: Zeina E. Jouni (zeina.jouni@kellog.com) or Sherry Tanumihardjo (sherry@nutrisci.wisc.edu)

UPCOMING EVENTS

March 27, 2015

CARIG Annual Conference, Boston, MA. Contact: Dr. Zeina E. Jouni, CARIG RIS Chair, **e-mail:** zeina.jouni@kellog.com (more information below)

March 28 - April 1, 2015

Experimental Biology 2015, Boston, MA. Contact: EB2014, FASEB Office of Scientific Meetings & Conferences, 950 Rockville Pike, Bethesda, MD

20814-3998, **website:** www.experimentalbiology.org
e-mail: eb@faseb.org (more information below)

June 24-26, 2015

Oxygen Club of California 2015 Congress, Valencia, Spain. **Website:** www.rosvalencia.edu or <http://oxyclubcalifornia.org>

July 8 -10, 2015

Macular Carotenoids Conference 2015. Cambridge, UK. Contact: Nutrasight Consultancy Ltd. (Conference Management), Carriganore House, Waterford Institute of Technology West Campus, Carriganore, Waterford, Ireland. Tel: +353 (0)51 302153. **Website:** www.macularcarotenoids.org
e-mail: info@ivr.ie

CARIG Events at Experimental Biology

Friday, March 27, 2015; 1:00 PM -5:00 PM

CARIG Annual Symposium

Location: Renaissance Waterfront Hotel, Atlantic Ballroom 2/3

Chair: Zeina E. Jouni,

Co-Chair: Sherry Tanumihardjo

1:00 - 1:10 PM: Introduction of the **James Allen**

Olson Memorial Lecture. Zeina E. Jouni, Kellogg Co.

1:10-2:00 PM: **J.A. Olson Memorial Lecture:** "Conversion of Dietary Carotenoids and Vitamin A into Bioactive Retinoids: Exploring Trails Blazed by Jim Olson." Earl Harrison, Ohio State University

CARIG Conference: Carotenoids, Retinoids and Cancer:

2:00-2:30 PM: *Retinoic Acid Biosynthesis Defects in Cancer.* Maureen Kane, University of Maryland

2:30-3:00 PM: *The Antioxidant Conundrum: Just Do It???* Harold Seifried, NCI-NIH

3:00-3:30 PM: Coffee Break

3:30-4:00 PM: *Tomato Carotenoids and Fatty Liver Disease.* Xiang-Dong Wang, Tufts University

4:00-4:30 PM: *Tomato Carotenoids and Risk of Prostate Cancer.* John W. Erdman Jr., University of Illinois Champaign-Urbana

4:30-5:00 PM: General Discussion

Friday, March 27, 5:00 – 6:30 PM

CARIG Steering Committee Business Meeting

Friday, March 27, 6:30 – 8:30 PM
CARIG Poster Competition and Reception
Location: Renaissance Hotel – Pacific Ballroom BC

Saturday, March 28, 10:30 AM – 12:30 PM
Minisymposium “Carotenoids and Retinoids in Human Health”.

Chair: Sherry Tanumihardjo
Co-Chair: Lisa Jahns
Student Chair: Jessica Cooperstone
Room: 156 A, Boston Convention Center

Sunday, March 29

Poster sessions:

Carotenoids and Health / Carotenoids & Retinoids
Molecular Mechanisms of Action and Vitamin A
Biofortification of Staple Crops with Micronutrients

FORTHCOMING / RECENT PUBLICATIONS

SIGHT AND LIFE Magazine 28 (2) 2014. PO Box 2116, 4002 Basel, Switzerland, **tel:** 41-61-815-8756, **e-mail:** klaus.kraemer@sightandlife.org **website:** www.sightandlife.org. See especially:

Li Y, Wongsirirot N, Blaner WS. Evolving insights into vitamin A transport, pp 36-43.

Letter to the Editor: Emerging science on lutein in the brain and why is nutrition so confusing? Hoppe PP, p 70.

Response to the letter from PP Hoppe. Johnson EJ, pp 71-73.

Carotenoids, inflammation and oxidative stress – implications of cellular signaling pathways and relation to chronic disease prevention. Kaulmann A, Bohn T. *Nutr Res* 34:907-29 (2014)

Review of methods for analysis of carotenoids. Amorim-Carrilho KT, Cepeda A, Fente C, Regal P. *TrAc Trends Anal Chem* 56:49-73 (2014)

Beta-cryptoxanthin as a Source of Vitamin A. Burri BJ. *J Sci Food Agr*, Epub 2014 Nov 5; DOI: 10.1002/jsfa.6942

Are biofortified staple food crops improving vitamin A and iron status in women and children? New evidence from efficacy trials. De Moura FF, Palmer AC, Finkelstein JL, Haas JD, Murray-Kolb LE, Wenger MJ, Birol E, Boy E, Pena-Rosas JP. *Adv Nutr* 5:568-70 (2014)

Risk assessment of -carotene in food supplements. The Norwegian Committee for Food Safety (VKM). VKM Report 2015:1:1-110. www.vkm.no/dav/e967639e8a.pdf

Alphabetical Listing of Recent Publications may be found at www.carotenoidsociety.org/articles-books-and-databases. It is prepared by Dr. Harold Furr, Department of Nutritional Sciences, University of Wisconsin, Madison.

TECHNICAL NOTES

Methods for analysis of carotenoids – a Review

This review covers current analytical techniques, instruments and methodologies used in analysis of carotenoids in foods and human samples. We also cover the importance of carotenoids in human health, carotenoid content in foods, bioavailability of carotenoids and evaluation of human intake of carotenoids. There is a wide variety of extraction methods and analytical techniques for determination of carotenoids. Recent advances in analytical instruments and the discovery of unknown metabolites of carotenoids widened the scope of carotenoid studies, especially through the application of metabolomics tools. Omics instruments and statistical methods perform untargeted and targeted profiling of carotenoids in foods and human samples, thereby advancing knowledge of their role in human health. Aimed at collating valuable information about recent analytical methodologies for carotenoids, this review mainly focuses on studies released in the past five years (2009-2013).

Amorim-Carrilho KT et al.
TrAC Trends Anal Chem 56:49-71(2014)

Development of lycopene micelle and lycopene chylomicron

The objectives of this study were to develop lycopene micelles and lycopene chylomicrons from tomato extracts for the enhancement and comparison of bioavailability. Lycopene micelles and chylomicrons were prepared by a microemulsion technique involving tomato extract, soybean oil, water, vitamin E and surfactant Tween 80 or lecithin in different proportions. The encapsulation efficiency of lycopene was 78% in micelles and 80% in chylomicrons, with the shape being roughly spherical and the mean particle size being 7.5 and 131.5 nm, respectively. A bioavailability study was conducted in rats by both gavage and intravenous administration, with oral bioavailability of lycopene, phytoene and phytofluene being 6.8, 4.3 and 3.1% in micelles and 9.5, 9.4 and 7.1% in chylomicrons, respectively. This outcome reveals high lycopene bioavailability through incorporation into micelle or chylomicron systems. Both size and shape should be considered for oral bioavailability determination. For intravenous

injection, lycopene micelles should be more important than lycopene chylomicrons for future clinical applications.

Chen YJ et al, 2014 *Nanotechnology* 25:155102.
DOI: 10.1088/0957-4484/25/15/155102

NEWS AND VIEWS

Effects of lutein and zeaxanthin on visual processing speed and efficiency

Lutein and zeaxanthin are major carotenoids in the eye but are also found in post-receptoral visual pathways. It has been hypothesized that these pigments influence the processing of visual signals within and post-retina, and that increasing lutein and zeaxanthin levels within the visual system will lead to increased visual processing speeds. To test this, we measured macular pigment density (as a biomarker of lutein and zeaxanthin levels in brain), critical flicker fusion (CFF) thresholds, and visual motor reaction time in young healthy subjects (n=92). Changes in these outcome variables were also assessed after four months of supplementation with either placebo (n=10), zeaxanthin only (20 mg/day; n=29) or a mixed formulation containing 26 mg/day zeaxanthin, 8 mg/day lutein, and 190 mg/day mixed omega-3 fatty acids (n=25). Significant correlations were found between retinal lutein and zeaxanthin (macular pigment) and CFF thresholds ($p < 0.01$) and visual motor performance (overall $p < 0.01$). Supplementation with zeaxanthin and the mixed formulation produced significant ($p < 0.01$) increases in CFF thresholds (~12%) and visual motor reaction time (~10%) compared to placebo. In general, increasing macular pigment density through supplementation (average increase of about 0.09 log units) resulted in significant improvements in visual processing speed, even when testing young, healthy individuals who tend to be at peak efficiency.

Bovier ER et al. *PLoS One* 2014 Sep 4;9(9):e108178
doi: 10.1371/journal.pone.0108178

Lutein decreases a marker of systemic inflammation

The purpose of this study was to investigate the effect of lutein on systemic complement activation in elderly individuals. Seventy patients with signs of early age-related macular degeneration (AMD) were included in this study. All subjects were randomly assigned to receive a 10 mg daily dose of lutein or a placebo for a time period of 1 year. EDTA blood was collected before and at various time-points during the study (0, 4, 8 and 12 months). The plasma level of the soluble complement membrane attack complex sC5b-9 was measured by ELISA. We found a significant 1.1 ng/ml monthly decrease in the plasma

sC5b-9 concentration in the lutein group ($p < 0.001$), resulting in a decrease from 60.3 ng/ml at baseline to 46.3 ng/ml at 12 months. For the placebo group, we found a significant 0.6 ng/ml monthly increase in plasma sC5b-9 concentration ($p = 0.001$), resulting in an increase from 51.6 ng/ml at baseline to 58.4 ng/ml at 12 months. Lutein supplementation inhibits the systemic activation of the complement system, which provides further functional evidence for the reported beneficial effects of this carotenoid in the management of AMD.

Tian Y et al. *Acta Ophthalmol* 93:141-5 (2015)

Lycopene Suppressed Hepatic Tumorigenesis in Mice

Obesity is associated with increased liver cancer risks and mortality. We recently showed that apo-10-lycopenoic acid, a lycopene metabolite generated by beta-carotene-9,10-oxygenase (BCO2), inhibited carcinogen-initiated, high-fat diet (HFD)-promoted liver inflammation, and hepatic tumorigenesis development. The present investigation examined the outstanding question of whether lycopene could suppress HFD-promoted hepatocellular carcinoma (HCC) progression, and if BCO2 expression is important using BCO2-knockout (BCO2-KO) and wild-type male mice. Results showed that lycopene supplementation (100 mg/kg diet) for 24 weeks resulted in comparable accumulation of hepatic lycopene (19.4 vs. 18.2 nmol/g) and had similar effects on suppressing HFD-promoted HCC incidence (19% vs. 20%) and multiplicity (58% vs. 62%) in wild-type and BCO2-KO mice, respectively. Intriguingly, lycopene chemopreventive effects in wild-type mice were associated with reduced hepatic proinflammatory signaling (phosphorylation of NK- B p65 and STAT3; IL6 protein) and inflammatory foci. In contrast, the protective effects of lycopene in BCO2-KO, but not in wild-type mice, were associated with reduced hepatic endoplasmic reticulum stress-mediated unfolded protein response (ER^{UPR}), through decreasing ER^{UPR}-mediated protein kinase RNA-activated like kinase-eukaryotic initiation factor 2 activation, and inositol requiring 1-X-box-binding protein 1 signaling. Lycopene supplementation in BCO2-KO mice suppressed oncogenic signals, including *Met* mRNA, -catenin protein, and mTOR complex 1 activation, which was associated with increased hepatic microRNA (miR)-199a/b and miR214 levels. These results provided novel experimental evidence that dietary lycopene can prevent HFD-promoted HCC incidence and multiplicity in mice, and may elicit different mechanisms depending on BCO2 expression.

Ip BC et al. *Cancer Prev Res* 7: 1219-27(2014)

Dietary tomato and lycopene impact gene expression during early prostate carcinogenesis

Consumption of tomato products containing the carotenoid lycopene is associated with a reduced risk of prostate cancer. To identify gene expression patterns associated with early testosterone-driven prostate carcinogenesis, which are impacted by dietary tomato and lycopene, wild type (WT) and transgenic adenocarcinoma of the mouse prostate (TRAMP) mice were fed control or tomato- or lycopene-containing diets from 4-10 weeks of age. Eight-week-old mice underwent sham surgery, castration, or castration followed by testosterone-repletion (2.5 mg/kg/d initiated 1 wk after castration). Ten week old intact TRAMP mice exhibit early multifocal prostatic intraepithelial neoplasia (PIN). Of the 200 prostate cancer-related genes measured by quantitative NanoString®, 189 are detectable, 164 significantly differ by genotype, 179 by testosterone status, and 30 by diet type ($P < 0.05$). In TRAMP, expression of *Birc5*, *Mki67*, *Aurkb*, *Ccnb2*, *Foxm1*, and *Ccne2* is greater compared to WT, and is decreased by castration. In parallel, castration reduces Ki67-positive staining ($P < 0.0001$) compared to intact and testosterone-repleted TRAMP mice. Expression of genes involved in androgen metabolism/signaling pathways are reduced by lycopene feeding (*Srd5a1*) and by tomato feeding (*Srd5a2*, *Pxn*, and *Srebf1*). Additionally, tomato feeding significantly reduced expression of genes associated with stem cell features, *Aldh1a* and *Ly6a*, while lycopene feeding significantly reduced expression of neuroendocrine differentiation-related genes, *Ngfr* and *Syp*. Collectively, these studies demonstrate a profile of testosterone-regulated genes associated with early stages of prostate carcinogenesis that are potential mechanistic targets of dietary tomato components. Future studies on androgen signaling/metabolism, stem cell features, and neuroendocrine differentiation pathways may elucidate the mechanisms by which dietary tomato and lycopene impact prostate cancer risk.

Wan L. et al. *Cancer Prev Res* 7:1228-39 (2014)

Retinoic Acid Regulates Hematopoietic Development from Human Pluripotent Stem Cells

The functions of retinoic acid (RA), a potent morphogen with crucial roles in embryogenesis including developmental hematopoiesis, have not been thoroughly investigated in the human setting. Using an *in vitro* model of human hematopoietic development, we evaluated the effects of RA signaling on the development of blood and on generated hematopoietic progenitors. Decreased RA signaling increases the generation of cells with a

hematopoietic stem cell (HSC)-like phenotype, capable of differentiation into myeloid and lymphoid lineages, through two separate mechanisms: by increasing the commitment of pluripotent stem cells toward the hematopoietic lineage during the developmental process and by decreasing the differentiation of generated blood progenitors. Our results demonstrate that controlled low-level RA signaling is a requirement in human blood development, and we propose a new interpretation of RA as a regulatory factor, where appropriate control of RA signaling enables increased generation of hematopoietic progenitor cells from pluripotent stem cells *in vitro*.

Rönn RE et al. *Stem Cell Reports* 4:269-81 (2015)

Internet Addresses for Carotenoid Researchers

1. USDA Nutrient Database for Standard Reference (SR 27) is a major source of food composition data for epidemiologists and nutritionists. The carotenoid database contains the best available estimates of carotenoid content in foods. The Agricultural Research Service (ARS) searchable database allows one to view carotenoid profile for more than 8,600 foods: www.ndb.nal.usda.gov/ndb/nutrients/index

2. International Carotenoid Society (ICS)
Website: www.carotenoidsociety.org

3. Carotenoid Section of the Lipid Database developed by Research Institute, International Medical Center of Japan webpage: www.lipidbank.jp
Also available on ICS webpage: www.carotenoidsociety.org through **Articles** button.

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Chair: Zeina E. Jouni (Battle Creek, MI)
Treasurer: Jessica Campbell (Minneapolis, MN)
Editor: Maria S. Sapuntzakis (Chicago, IL)
E-mail: msapuntz@gmail.com
Website: www.carotenoidsociety.org/news-views-and-opinions