



CEG emeritus member [Daniel W. Nebert, M.D.](#), is lead author of an extensive review of the updated “SLC39A8 story”: **Nebert DW, Liu Z. SLC39A8 gene encoding a metal ion transporter: discovery and bench to bedside. Hum Genomics. 2019 Sep 14;13(Suppl 1):51. PMID: 31521203; PMCID: PMC6744627.**

*SLC39A8* is an evolutionarily highly conserved gene encoding the ZIP8 metal cation transporter in all vertebrates. *SLC39A8* is expressed in every cell type examined, including pluripotent embryonic stem cells. Uptake of ZIP8-mediated  $Mn^{2+}$ ,  $Zn^{2+}$ ,  $Fe^{2+}$ ,  $Se^{4+}$ , and  $Co^{2+}$  represents its endogenous functions – moving these cations into the cell. By way of mouse genetic differences, the trait of “subcutaneous cadmium-induced testicular necrosis” was assigned to the *Cdm* locus by the Ben Taylor lab in the 1970s. This led to identification of the mouse *Slc39a8* gene, its most closely related *Slc39a14* gene, and creation in the Nebert lab of *Slc39a8*-overexpressing and *Slc39a8*-underexpressing mouse lines; the *Slc39a8*(-/-) global knockout mouse is early-embryo lethal. The *Slc39a8*-underexpressing mutant animals die between gestational day 16.5 and postnatal day 1 – exhibiting severe anemia; lack of normal blood cell production; smaller-than-normal spleen, heart, kidney, lung and liver, stunted growth, and smaller deformed legs. Not surprisingly, genome-wide association studies subsequently revealed human *SLC39A8*-deficiency variants exhibiting innumerable defects correlated with clinical disorders in virtually every organ, tissue, and cell-type. The Nebert lab thus began in the mid-1990s with a “toxicology trait” (testicular necrosis within 48 h, caused by cadmium given subcutaneously); then identified the responsible gene, which encodes a divalent cation transporter; then discovered the multiple functions of this transporter in virtually every cell-type in the body; to ultimately realizing (when the gene is underexpressed) how important it is in virtually every field of medicine. Clinical traits with which *SLC39A8*-deficiency variants are (so far) associated include, but are not limited to,  $Mn^{2+}$ -deficient hypoglycosylation; decreased serum high-density lipoprotein-cholesterol levels; decreased height, increased body mass index; greater risk of coronary artery disease, hypotension, cardiovascular death, allergy, ischemic stroke, Parkinson disease, inflammatory bowel disease, adolescent idiopathic scoliosis, and systemic lupus erythematosus with primary Sjögren syndrome; and “inadvertent participation” in the inflammatory progression of osteoarthritis.

We seek to highlight *all* CEG member activity and successes. [Share your news with us](#) so we can share it with others!



## U.S. Congressional Staff Briefed on PFAS Exposure

In the 2nd US. Capitol Hill appearance by a CEG representative in as many weeks, Director Susan M. Pinney, Ph.D., F.A.C.E., was invited to speak on “Health Effects of PFAS Exposure on Women and Children” at an hour-long

October 3, 2019, Congressional briefing in Washington, DC. The event was sponsored by the Environmental Working Group ([www.ewg.org](http://www.ewg.org)). Pinney also met with staff and leaders in seven Congressional offices to discuss this important water quality and public health concern.

## Recently Published

Gulati S, Desai J, Palackdharry SM, Morris JC, Zhu Z, **Jandarov R**, et al. Phase 1 dose-finding study of metformin in combination with concurrent cisplatin and radiotherapy in patients with locally advanced head and neck squamous cell cancer. *Cancer*. 2019 Oct 18. [PMID: 31626727](#)

**Genter MB**, Doty RL. Toxic exposures and the senses of taste and smell. *Handb Clin Neurol*. 2019;164:389-408. [PMID: 31604559](#)

## NIEHS Honors Worker Safety and Health Pioneer Carol Rice, Ph.D.

[NIEHS has honored with a public profile CEG emeritus member Carol Rice, Ph.D.](#), a nationally respected pioneer in worker health and safety training. Rice began her distinguished career in industrial hygiene in 1975; since 1987 she has directed the [Midwest Consortium for Hazardous Waste Worker Training](#), which now reaches up to 17,000 people each year. The program enhances the safety and health of workers and community members in 9 states, including OH, KY, IN, IL, MI, MN, ND, TN and WI.



## Coming Up

**Pilot Funding Opportunity:** The next CEG pilot research funding announcement (RFA) will be posted online and sent directly to members in early December. Application criteria are likely to be similar to those enumerated in prior announcements; investigators planning a Year 28 proposal might wish to view the previous RFA, still accessible [here](#).

**Save the Date:** CEG Research Symposium, Thurs-Fri February 20-21, 2020. Keynote speaker TBA. Stay tuned!