2019 SOT *In Vitro* Toxicology Lecture and Luncheon
Student Discussion Guide

Patient-Based Cellular Model Systems to Assess Individual Risk to Neurotoxicants

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Collectively, an individual's genetics, environmental exposure history, and the effects of aging can contribute to brain disease etiology. Each of these factors can be difficult to model using *in vivo* animal models. This lecture suggests that patient-based (individual-based) cellular model systems, such as human induced pluripotent stem cells (iPSCs), enable characterization of personalized toxicological susceptibility.

- A ***gene-environment interaction*** (GxE) is when two different genotypes respond differently to an environmental exposure. For example, individuals with mutations of the PARK2 gene are sensitive to copper exposure
- Human ***induced pluripotent stem cells*** (iPSCs) are reprogrammed cells from an adult individual that have the potential to become any other cell type in the body. For example, human skin cells can be "reprogrammed" into neurons.

General Discussion: Parkinson's and neurodegenerative diseases are not the only type of disease that could benefit from iPSCs models. As a group discuss different types of GxE that can underlie disease and how iPSCs could be leveraged for characterizing personalized susceptibility.

Developing an effective iPSC model requires knowledge about the disease. Discuss the features of an appropriate iPSC disease model by considering the following:

(1) Are there characteristics of individuals, populations, sub-populations, or risk groups that would be critical in the identifying whom to select for generation of a stem cell-based model system of the disease?

(2) Is there a target cell type primarily impacted or contributing to pathogenesis?

(3) Are there known or suspected toxicants that contribute to disease risk?

(4) Are there particular developmental stages or sequential time points that are important in the pathogenesis?

(5) Are there genetic-based animal models that recapitulate human pathogenesis?