SOT *In Vitro* Lecture 2016

Table Discussion Activity

Choice of a model system for any biological study is crucial. In toxicology, choice of model can vastly alter results. The ultimate goal is to better understand how a toxicant will impact the exposed organism. We can gain valuable insight into *in vivo* exposure through use of *in vitro* models.

Cells interact with other cells in tissues in a variety of ways and often that interaction is crucial for normal physiological function. The co-culture model discussed by Dr. Kaminski shows how multiple cells grown in culture together can better reflect the impact of toxicants on tissues than individual cell types.

A brief list of some of the ways that cells can interact:

- Production of extracellular signals (cytokines, hormones, growth factors, local mediators, cAMP, neurotransmitters, nitric oxide, etc)
- Production of proteins for activation of other cells
- Production of proteins for repression of other cells
- Acting as a scaffold or secreting extracellular matrix
- Antibody/Antigen presentation
- Triggering apoptosis or survival
- Expression of surface proteins for cell:cell interaction (i.e.,receptor:ligand)

A specific example of an interaction in toxicology that might be best studied with a co-culture model:

In vivo, B cell secrete antibodies directed against antigens to protect host from pathogens. Once B cells have bound a specific antigen, interaction with Type 2 T helper (Th2) cells through CD40-CD40L provide key signals for B cell differentiation into plasma cells that produce antibodies.

B cells grown *in vitro* alone lack these key signals for differentiation, which impacts their response to toxicant exposure. B cells grown in co-culture with Th2 cells, or irradiated fibroblasts expressing CD40L cells allows for differentiation of B cells into antibody secreting cells. The response to toxicant exposure with and without differentiation can be examined using this co-culture model.

There are other types of co-cultures models that may be used in the study of toxicology including:

- Airway epithelial cells and alveolar macrophages
- Intestinal epithelial cells and peripheral blood mononuclear cells
- Brain capillary endothelial cells and astrocytes
- Fibroblasts and keratinocytes
- Granule neurons and astrocytes
- Hepatocytes and non-parenchymal cells

A few final thoughts before you try to apply what you learned. Participants experience with these types of systems will be varied. However you don't have to have used a co-culture model to think about how it might be different from other studies you have completed. Apply your knowledge of basic biology to the questions at hand. Don’t be afraid to throw ideas out at your table for discussion.

Thought questions:

1) Does using more than one cell type in an *in vitro* co-culture model more closely mirror biological processes seen *in vivo*? Why or why not?

2) What controls should be considered for experiments using two different cell types in toxicology? (Hint: there may be quite a long list of appropriate controls) How does choosing the correct control influence your data interpretation?

3) How does the co-culture system described by Dr. Kaminski allow researchers to apply the 3Rs (reduce, refine, replace) of animal research?