AN MSBSS WEBINAR

# SUCCESSFUL AWARD APPLICATIONS

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# What We Will Cover Today

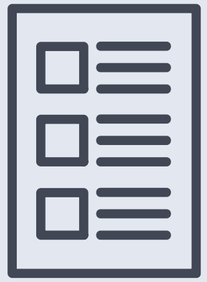
## ESSENTIAL KNOW-HOW

The extended abstract
Recommendation letters
Other tips & tricks
How are applications reviewed?

## 1ST RULE OF AWARD APPLICATIONS

# APPLY FOR EVERY AWARD YOU ARE QUALIFIED FOR.

IT'S LIKE THE LOTTERY: YOU CAN'T WIN IF YOU DON'T PLAY.



# THE EXTENDED ABSTRACT

An example of a successful award application

# Extended abstract

## 1-2 PAGES

### PROBLEM FORMULATION 1

1st few sentences of your application
What problem is your project trying to solve?

### BACKGROUND MATERIAL 2

This section provides the reader with some context to better understand why this is such an important research question to tackle

### STATEMENT OF PURPOSE 3

What's this project for, anyway?

**Population Variability in Neurotoxicity Outcomes Modeled In Vitro with Diversity Outbred Neural Progenitor Cells**

Dahea You[1], Mamta Behl[1], Ted Choi[2], Lesley Page[2], Logan Everett[3], Michele Balik-Meisner[3], Devin Porter[2], Kristine Witt[1], Richard Paules[1], Alison H. Harrill[1]

[1]National Institute of Environmental Health Sciences, RTP, NC, USA
[2]Predictive Biology, Carlsbad, CA, USA
[3]Sciome LLC, RTP, NC, USA

1 Developmental neurotoxicity (DNT) is a critically important area of investigation, yet it remains one of the most challenging health effects of chemicals to study. To date, there are few screens for DNT and existing assays do not incorporate sufficient genetic diversity to capture variations in
2 DNT susceptibility across individuals in diverse populations. In risk assessment, a default uncertainty factor of 3.16 has been applied to account for interindividual variability in toxicodynamics and to provide a margin of safety for susceptible subpopulations in setting the human reference dose. However, studies have indicated that this default factor may be under-protective for chemicals that exhibit a wide toxicodynamic range across individuals. The use of an experimentally derived toxicodynamic variability factor (TDVF) has been suggested to replace the traditional uncertainty factor. A TDVF is a chemical specific adjustment factor that quantifies interindividual differences in responses based on the chemical-specific data collected across a population of individuals. A TDVF can further reduce the uncertainty on interindividual differences and provide more reliable information to the risk assessors on population-wide differential sensitivity and safe levels of exposure to chemicals. Such an approach is especially
3 critical in assessing DNT, where multiple factors can modulate susceptibility. To determine chemical-specific toxicodynamic variability for DNT under human-relevant exposure conditions, we developed a screening assay utilizing the Diversity Outbred (DO) mouse population to account for population differences in susceptibility.

PARAGRAPH 1

# Extended abstract

## 1-2 PAGES

### DESCRIBE THE EXPERIMENT 1

This should be concise, with just enough detail to understand the experiment

### FINDINGS 2

This section provides the reader with some context to better understand why this is such an important research question to tackle

### FINDINGS IN CONTEXT 3

How do your findings relate to real-world applications?

The DO mice were created as a population resource composed of genetically unique individuals with a highly randomized allelic architecture [1, 2]. DO mice can act as a population surrogate for human epidemiological studies, allowing investigators to query toxicodynamic variability in responses and their genetic drivers. In this study, we utilized 100 male and 100 female neural progenitor cell (NPC) lines derived from the DO population to assess the population-wide variability upon exposure to the chemicals. DO NPCs were exposed to one of six chemicals at 12 concentrations (0-200 μM): rotenone, dieldrin, estradiol, methyl mercury, 2,2',4,4',5-pentabromodiphenyl ether (BDE99) or isopropylated phenyl phosphate (IPP). Chemicals tested in this study were the known neurotoxic agents with available *in vivo* mouse data to compare. Cell viability was measured at 114 h post-exposure using the Alamar blue assay. We observed wide distributions of log-transformed cytotoxicity EC10 for rotenone and methyl mercury, indicating the contribution of genetic variants to inter-individual sensitivities to the chemical agents (**Figure 1**). A Bayesian probabilistic approach [3] was used to calculate a chemical-specific TDVF to quantitatively estimate the variability in the population dose-response and confidence intervals around the variability (**Table 1**). Our data demonstrated that the default uncertainty adjustment factor would likely be inadequate to account for interindividual differences in sensitivity to cytotoxicity associated with rotenone and methyl mercury chloride, whereas the default value may be adequately protective for the remaining tested chemicals. In addition, the mouse-derived TDVFs were comparable to human-derived TDVFs calculated from human lymphoblastoid cell lines exposed to the same chemicals, suggesting that TDVFs derived from DO NPCs can be translated to human variability [3].

PARAGRAPH 2

### 4 HUMAN RELEVANCE

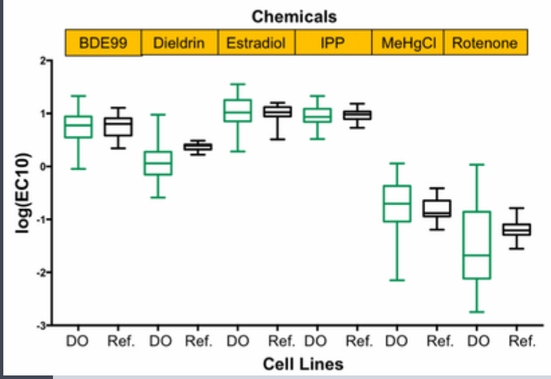



**Figure 1. Toxicodynamic variability to test agents in a pilot study.** Log-transformed EC10 (μM) ranges of the cytotoxicity of DNT agents at 114 h are compared between the reference cell line (Ref., black), which is a single DO NPC line, and male and female DO NPC population (DO, green). Most distributions are approximately normal. From these data, we observed that rotenone and methyl mercury display wide interindividual toxicodynamic variability.

## FIGURE 1

Including a figure brings your research to life!

**And,** saves you text space because you can summarize results and point to figure.

| Chemical | | IPP | Estradiol | BDE99 | Dieldrin | Rotenone | MeHgCl |
|---|---|---|---|---|---|---|---|
| TDVF | Mouse DO NPCs (90% confidence interval) | 1.71 (1.60, 1.86) | 1.82 (1.66, 2.05) | 2.39 (2.00, 2.96) | 2.8 2.42, 3.33) | 11.2 (7.51, 19.1) | 26.9 (10.3, 109) |
| | Human lymphoblastoid cell lines[3] | - | - | - | 3.76 | - | 16.03 |

**Table 1.** DO Toxicodynamic variability factors (TDVF) and confidence intervals for cytotoxicity of the DNT agents at 114 h. – indicates no available human data

## TABLE 1

Similarly, a table can really drive home your main points.

Can be very concise with an inline legend.

# Final Conclusion

## WHAT DO YOUR RESULTS IMPLY?

1. Explain why we should be excited about what you found

## FUTURE DIRECTIONS

Whats the next step to advance this research? 2

1 Collectively, these results suggest that the DO NPC lines can serve as a testing platform to assess toxicodynamic variability of DNT relevant to the human population. In the next phase of our studies, TempO-seq transcriptomic analysis of the samples is ongoing to analyze differentially expressed genes and associated pathways and determine the mechanisms underlying the susceptibility to methyl mercury toxicity. A classification and regression tree machine learning assessment will be utilized to identify sensitive biomarkers that can predict the adverse neurotoxic outcome. Taken together, this population-based *in vitro* assay using the DO mouse population will 3 provide a data-driven estimate for interindividual toxicodynamic variability suitable for improved risk assessment and more precise determination of human reference doses.

PARAGRAPH 3

3

## PUTTING IT ALL TOGETHER

You'll notice that the first sentence and last sentence of the paragraph aren't materially different

# References

## KEEP THESE TO A MINIMUM

They can quickly eat up space

But, these can give reviewers the impression that your arguments are well-supported by prior data

**References:**


1. Collaborative Cross, C., *The genome architecture of the Collaborative Cross mouse genetic reference population.* Genetics, 2012. **190**(2): p. 389-401.
2. Svenson, K.L., et al., *High-resolution genetic mapping using the Mouse Diversity outbred population.* Genetics, 2012. **190**(2): p. 437-47.
3. Chiu, W.A., F.A. Wright, and I. Rusyn, *A tiered, Bayesian approach to estimating of population variability for regulatory decision-making.* ALTEX, 2017. **34**(3): p. 377-388.

# Use restraint

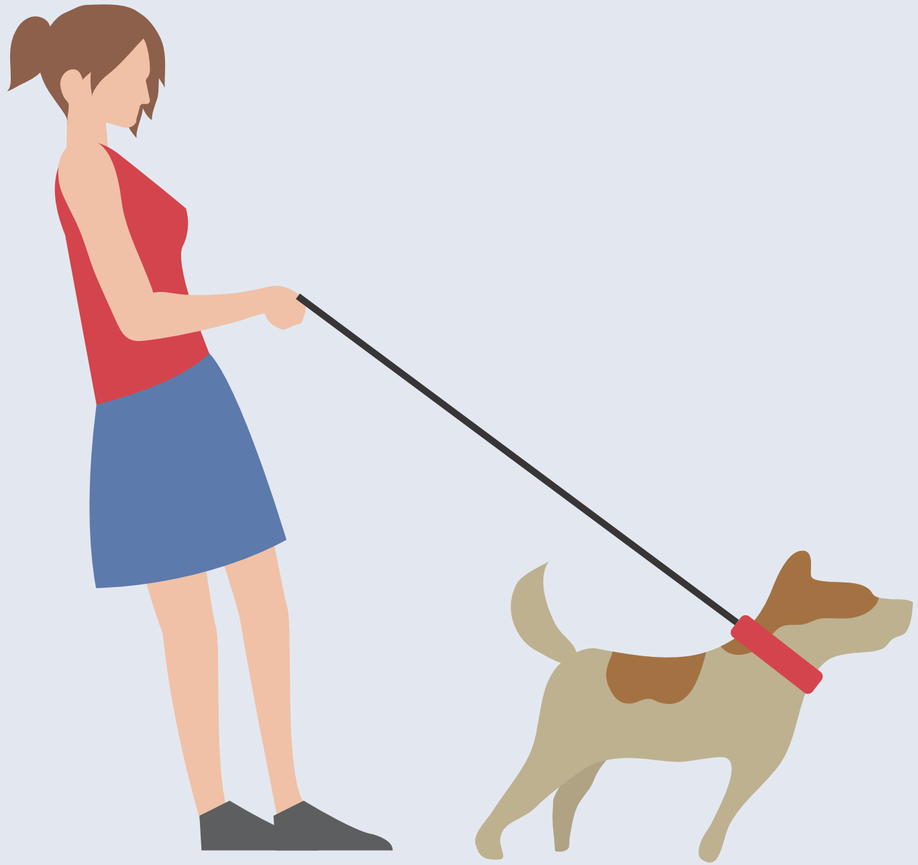
## RESIST TEMPTATION

You want to impress the judges and might think: "They want to hear about everything I've ever done in this lab!!"

They **don't**.

What they want is a coherent story.

You can always show your shiny new data in your talk or poster at the meeting.



# TIPS & TRICKS

## REVIEW EXAMPLES

Ask your mentors, friends, and colleagues for examples of successful applications.

## DON'T GO IT ALONE

Ask your mentors and peers to review and provide feedback.

## PLAN AHEAD

Check ALL submission dates and requirements. It takes time to develop concise documents. Plan for a few drafts.

## TAKE IT SERIOUSLY

Extended abstracts are reviewed in detail and often discussed by the review panel.

# Recommendation letters

THE ONE PIECE WE CAN'T CONTROL

LET'S REVIEW WHAT MAKES A GOOD LETTER.

SOMEDAY YOU'LL HAVE TO WRITE ONE!

# Key Elements

## MAKE YOUR LETTER POP

### HOW DO YOU KNOW EACH OTHER?

"Edgar has been a graduate student in my lab for 3 years"

"I've gotten to know Yoselin well over the 6 months she has spent as a postdoc fellow in my group"

### EXAMPLES OF HOW THEY STAND OUT?

"Ari is a team player - he always goes out of his way to help other lab members with their experiments."

"Emily has actively sought leadership opportunities in the SOT and on campus, for example..."

### SPECIFIC CONTRIBUTIONS TO THE WORK

"Sam picked up the experiment from a former postdoc, but has worked tirelessly for the past year to make it their own by updating and implementing a new RNAseq analysis pipeline."

# STAGES OF REVIEW

## 1. REVIEWERS ASSIGNED

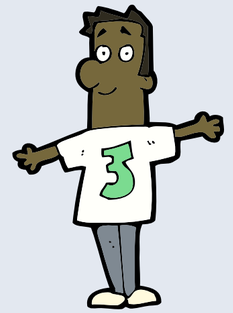
Depending on how many applications, they may be divvied up across a few reviewers.


## 2. APPLICATIONS SCORED

Blinded scoring system (often 0-10) for main elements, such as novelty and importance of work, clarity of written elements, strength of recommendation.


## 3. APPLICATIONS DISCUSSED

Often if avg. scores are close for the top few applicants, a call will be convened to discuss and gain agreement on the winner.



# FINAL THOUGHTS

## PERSIST

You won't get every award you apply for and that's OK.

## BLINDERS ON

Every research project and experience is different. Don't compare your research to another's - you have a shot!

## RELATIONSHIPS

The key to a great recommendation letter is to develop a consistent positive relationship with a mentor.

## SURVEILLANCE

Check society websites and social media for award announcements. Check your institution's fellows' office too!

# GOOD LUCK!

"Give it your best!" - Alison Harrill