Message

From: Pham, Nathalie@OEHHA [Nathalie.Pham@oehha.ca.gov]
Sent: 7/2/2019 11:07:37 PM
To: Paul-Friedman, Katie [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9de6209426a941908301318615f5507b-Paul-Friedm]
CC: Sun, Meng@OEHHA [meng.sun@oehha.ca.gov]
Subject: RE: Cytotoxicity cutoff for ToxCast/Tox21 data

Hi Katie --

It is a pleasure to e-meet you. Thank you for the clarification on the cytotoxicity threshold currently on the dashboard. I had a couple of follow-up questions per your earlier email that I was hoping you could answer --

- Do you know which chemicals have been screened through all 88 assays or how we could find that information? Is there a list of the 88 assays or would we just look at individual assay design/biological process target?
- In the past, I remember there was material stating 3 MADs from the cytotoxicity limit was a good rule of thumb for specificity of an assay hit. Is that still an applicable rule?

Thanks Katie,

Nathalie

From: Sun, Meng@OEHHA <meng.sun@oehha.ca.gov>
Sent: Tuesday, July 2, 2019 9:27 AM
To: Paul-Friedman, Katie <Paul-Friedman.Katie@epa.gov>; Williams, Antony <Williams.Antony@epa.gov>
Cc: Pham, Nathalie@OEHHA <Nathalie.Pham@oehha.ca.gov>
Subject: RE: Cytotoxicity cutoff for ToxCast/Tox21 data

Hi Katie and Tony,

Thank you both very much for the publication and explanation. Now we have a better understanding for the cytotoxicity threshold. I'd like to introduce my colleague Nathalie Pham. She also uses ToxCast data frequently and may reach out to you for technical questions. We really appreciate your help with our use of the Chemicals Dashboard.

Best,
Meng

From: Paul-Friedman, Katie <Paul-Friedman.Katie@epa.gov>
Sent: Monday, July 1, 2019 6:32 PM
To: Williams, Antony <Williams.Antony@epa.gov>; Sun, Meng@OEHHA <meng.sun@oehha.ca.gov>
Subject: RE: Cytotoxicity cutoff for ToxCast/Tox21 data

Hi Meng and Tony,

Yes, the publication that Tony referenced provides a detailed description of the calculation. Currently there are 88 cytotoxicity assays that can be included in the cytotoxicity threshold computation (though not all chemicals have been screened in all 88). The cytotoxicity threshold that appears on the Dashboard is actually the lower bound on the prediction of the median cytotoxicity, so it will appear lower than many of the hits. We do not currently filter out any data; the cytotoxicity threshold is truly more for context in terms of identifying activity that looks like it occurs "specifically," i.e. less likely to be confounded by cytotoxicity. Obviously any filtering applied by a user should be context specific. I'm happy to dive deeper into this and the computation itself with you if you have some more specific questions. Please reach out anytime.

Kind regards,
Katie

Katie Paul Friedman, PhD
Toxicologist
National Center for Computational Toxicology
Office of Research and Development
U.S. Environmental Protection Agency
RTP D120C
Research Triangle Park, NC 27711
Phone: 919-541-0660
paul-friedman.katie@epa.gov

From: Williams, Antony
Sent: Monday, July 1, 2019 8:39 PM
To: Sun, Meng@OEHHA <meng.sun@oehha.ca.gov>
Cc: Paul-Friedman, Katie <Paul-Friedman.Katie@epa.gov>
Subject: RE: Cytotoxicity cutoff for ToxCast/Tox21 data

Meng,

Thank you for your email. While I can take a poke at a number of your questions I believe that the publication at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6280881/ will cover a number of your questions. My colleague Katie Paul-Friedman is far more familiar with the data and details of determining the cytotoxicity limits and I have cc'ed her on this email as her responses will offer way more detail than I can provide. Best wishes.

Antony J. Williams
National Center for Computational Toxicology
U.S. Environmental Protection Agency
109 T.W. Alexander Drive
Room D131I, Mail Drop D143-02
Research Triangle Park, NC 27711

Office Phone: 919-541-1033
Mobile Phone: Personal Matters / Ex. 6

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From: Sun, Meng@OEHHA <meng.sun@oehha.ca.gov>
Sent: Monday, July 1, 2019 2:07 PM
To: Williams, Antony <Williams.Antony@epa.gov>
Subject: Cytotoxicity cutoff for ToxCast/Tox21 data

Hi Tony,

I hope you are doing well. This is Meng from OEHHA at Cal/EPA. My colleagues and I have some additional questions regarding the Chemicals Dashboard. It is such a great resource and we are trying to make the best use out of it.

Our questions are: how do you calculate the single cytotoxicity cutoff that appears on the "chemical activity summary" chart? Is it based on a combination of the variability assay results? Do you use this cutoff to filter out any assays? For example, the cytotoxicity cutoff for 4-aminophenol is very low (8.22 µM) and a lot of the current "positives" have an AC50 of higher than 20 or even 50 µM. When we checked individual variability assays, the AC50s look more comparable

to the AC50s of the "real signal" such as ER inhibition. We are trying to tease out the cytotoxic effect from specific receptor antagonism, and wonder if we can use this cutoff or should check individually paired variability assay results.

Thank you very much!

Meng

Meng Sun, M.S., Ph.D.
Staff Toxicologist (Specialist)
Cancer Toxicology and Epidemiology Section
Office of Environmental Health Hazard Assessment (OEHHA), CalEPA
Phone: (916) 327-7327
Fax: (916) 327-7340

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