

Guidance for Using the View Audit Feature in IRBManager

Note this feature will work for all xForms in IRBManager

This guidance will help you use the View Audit feature in IRBManager, which will show changes made within any xForm section.

1. After opening an xForm in IRBManager, go to the form section in which you want to review changes.

SECTION C ~ PROTOCOL SUMMARY

C.1: Provide a brief non-scientific summary of the aims and objectives of this protocol in language understandable to a high school senior. This should be summary of your research that you or the University could provide to the public. DO NOT include details of procedures here. [Add Note](#) [View Audit](#)

Entered: 02/11/2021 By: Wilson, Tracee Internal: No

C1: The summary provided is very technical and not written for non scientific. The summary describes the previous work done by this laboratory but does not really explain the rationale for creating new crossing with different mice. Please clarify the aims of the proposal and the rationale.

There is a mention of SV40T (TAg) animals in the summary but the nature of this mutation remains unclear as to how it incorporates into the whole of the study. Please clarify.

Section C.1. Requests that the PI provide a brief non-scientific summary of the aims and objectives of this protocol in language understandable to a high school senior. Please reconsider the verbiage in this section and provide the type of response requested.

response to reviewer comments: per comment, I modified the content to be less scientific. I did not elaborate the portion on SV40T, nor any of the mutations which are scientific.

2. In the top right-hand corner of the selected section, select "View Audit".

[View Audit](#)
[Include details](#)

3. The audit will provide a complete list of all changes made to that section. Removed items will be listed in red and will be crossed out, and added items will be listed in green and underlined. The most current information for this audit will be at the top of the list.

When / Who	Change
	<p>Edited summary:</p> <p>Our research lab is interested in understanding the cellular mechanisms underlying neurological disorders such as Alzheimer's disease. Understanding the cellular mechanisms involved in the disease process is a necessary step in developing successful therapy for delaying or halting the cognitive and neurological declines in affected individuals. Our study is focused on evaluating the role of neuronal cell cycle activation as an Alzheimer's disease mechanism. We are utilizing our unique mouse model of neuronal cell cycle re-entry in combination with other transgenic mice to accomplish our research goal.</p> <p>Alzheimer's disease is characterized by two distinct protein pathologies, amyloid beta and tau pathologies. The aim of this project is to evaluate the role of neuronal cell cycle re-entry (NCCR) on 1) human amyloid beta, 2) human tau and 3) to evaluate the interaction between AD-relevant amyloid and tau pathologies using our mouse model. We hypothesize that cell cycle activation in the presence of humanized forms APP and tau proteins, which are processed to generate amyloid and tau pathologies respectively, will lead to a closer replication of the plaque and tangle pathologies seen in human AD brains. Furthermore, evaluation of our animal models will help us identify NCCR-mediated pathophysiological mechanisms involved in the development of AD-relevant amyloid and tau pathologies.</p>
02/27/2021 11:21 AM ET	<p>response to reviewer comments: per comment, I modified the content to be less scientific. I did not elaborate the SV40T, nor any of the mutations which are scientific.</p> <p><u>Edited summary:</u></p> <p>Our research lab is interested in understanding the cellular mechanisms underlying neurological disorders such as Alzheimer's disease. Understanding the cellular mechanisms involved in the disease process is a necessary step in developing successful therapy for delaying or halting the cognitive and neurological declines in affected individuals. Our study is focused on evaluating the role of neuronal cell cycle activation as an Alzheimer's disease mechanism. We are utilizing our unique mouse model of neuronal cell cycle re-entry in combination with other transgenic mice to accomplish our research goal.</p> <p>Alzheimer's disease is characterized by two distinct protein pathologies, amyloid beta and tau pathologies. The aim of this project is to evaluate the role of neuronal cell cycle re-entry (NCCR) on 1) human amyloid beta, 2) human tau and 3) to evaluate the interaction between AD-relevant amyloid and tau pathologies using our mouse model. We hypothesize that cell cycle activation in the presence of humanized forms APP and tau proteins, which are processed to generate amyloid and tau pathologies respectively, will lead to a closer replication of the plaque and tangle pathologies seen in human AD brains. Furthermore, evaluation of our animal models will help us identify NCCR-mediated pathophysiological mechanisms involved in the development of AD-relevant amyloid and tau pathologies.</p>
02/26/2021 7:00 PM ET	<p>Our research lab is interested in understanding the cellular mechanisms underlying neurological disorders such as Alzheimer's disease. Understanding the cellular mechanisms involved in the disease process is a necessary step in developing successful therapy for delaying or halting the cognitive and neurological declines in affected individuals. Our study is focused on evaluating the role of neuronal cell cycle activation as an Alzheimer's disease mechanism. We are utilizing our unique SV40T mouse (TAg) model knock-out <u>knock-in</u> of neuronal cell cycle re-entry in combination with other transgenic mice to accomplish our research goal. When TAg and Off mice are genetically combined by breeding (TAg/Off mice), we are able to modulate temporal-expression patterns of SV40T in neurons by providing rodent chow either containing or lacking doxycycline, an antibiotic. In the context of <u>The aim of this project is to evaluate the role of neuronal cell cycle dysregulation/entry in (NCCR) adult humanized 1) APP human knock-in amyloid mice (beta, 2) human tau and humanized tau knock-in mice will produce plaques and tangles, respectively, in animals that normally do not show Abeta and tau aggregation. Alzheimer's disease (AD) is characterized/evaluate by the three (interaction main pathological hallmarks: amyloid plaques, neurofibrillary tangles (NFT), and neuronal loss. Our published study demonstrates that persistent SV40T-mediated cell cycle activation in mature neurons produce endogenous between AD-relevant amyloid and tau pathologies and neuronal loss in mice. (Park et al., 2007; Park and Barrett, 2020). However, the neuropathology using our mice did not fully resemble the plaque and tangle features of amyloid and tau pathology observed in AD; dense-core plaques and MCI-specific conformational tau, respectively. We postulate that this is likely due to differences between mouse vs. human APP and tau protein model. We hypothesize that cell cycle activation in the presence of humanized forms of APP (App-KI mice) and Tau (hTau-KI mice) proteins will lead to a closer replication of the plaque and tangle pathologies seen in human AD brains. Furthermore, evaluation of our animal models will help us identify genetic mechanisms involved in the development of AD-relevant amyloid and tau pathologies. We are currently evaluating various NCCR-mediated APP pathophysiological mechanisms involved in the development of AD-relevant amyloid and tau pathologies in KI mice with TAg and Off mice to generate necessary double, triple, and quadruple transgenic mice (e.g. TAg/Off, TAg/Off/AppNL-KI, TAg/Off/AppNL-KI, TAg/Off/hTau-KI, TAg/Off/AppNL/hTau-KI, TAg/Off/AppNL/hTau-KI).</u></p>