Exploration of the Auditory System and the Prevention of Hearing Loss from Chemotherapy

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Introduction

Cisplatin is one of the most common chemotherapeutic drugs prescribed by doctors around the world, however among the drug's many side effects is an increase of ROS levels in the body. This results in mitochondrial destruction which causes damage to the auditory system and hearing loss. However, *Honokiol,* a traditional Chinese drug with mitochondrial protection and anti-tumor properties has been shown to prevent hearing loss from Cisplatin. This study aims to identify the effects of Cisplatin and *Honokiol* on the auditory system through hearing tests and analysis of the inner ear on a cellular and subcellular level in order to determine the mechanisms and sites of action for these drugs. The X-Ray Fluorescence method is used as a mepping technique on a nanometer scale in order to achieve this goal. The research conducted in this study has also allowed us to gain a greater understanding of the parts of the auditory system and how it functions.

Methods & Materials

- Mice treated with varying concentrations of cisplatin and *Honokiol.*
- Hearing ability of the mice determined through hearing tests at preselected increments of time.
- Samples of the cochlea and inner ear are taken and put through an X-Ray Fluorescence Microscopy
- Results from both the hearing tests and microscopy are analyzed to see how the drugs are affecting the auditory system and understand how this system functions and changes due to external factors.

Honokiol Prevents Cisplatin Induced Hearing Loss

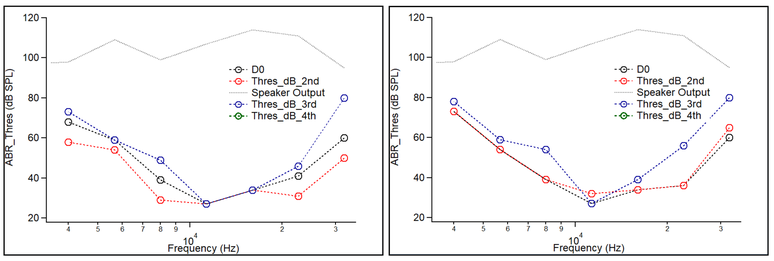
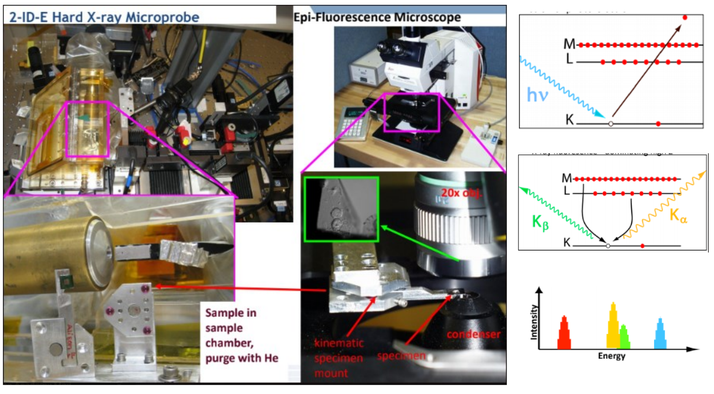


Figure 1 shows the hearing test results from mouse HNK164 who was treated with 15 mg/kg of cisplatin, and 10 mg/kg of *Honokiol*. Figure 2 shows the hearing test results of mouse HNK163 who was treated with just 15 mg/kg of cisplatin. The images demonstrate how treatment with *Honokiol* results prevents the hearing loss side effect from cisplatin.



The figures above show the XFM machine and the important parts of this mechanism including the sample chamber, X-ray microprobe with the X-Ray beam and the Epi-Fluorescence microscope which are all used in the XFM process. On the right are three diagrams that demonstrate the science behind the XFM and explain how this method works and quantifies elements. The images explain how the X-Ray beam pushes out an electron, requiring an electron from an outer shell to take its place and creating a change in energy which can they be quantified and analyzed for the purpose of the study.

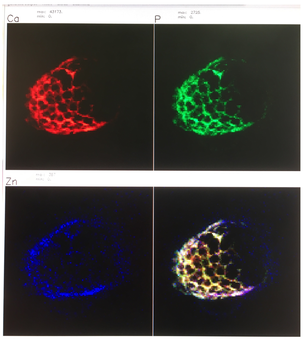


Figure 3 shows an XFM scan of a section through the middle ear ossicle, the incus, of a 5 day old mouse. The upper left panel shows the concentration of calcium, right upper shows phosphorus and left lower shows zinc. The right lower panel is a combination of the three to demonstrate colocalization.

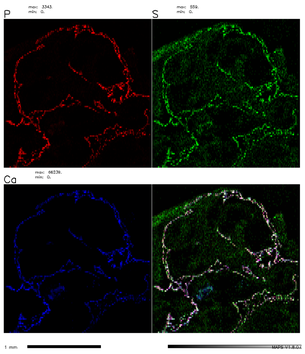


Figure 4 shows a cochlear cross section sample and highlights concentrations of phosphorus, sulfur and calcium in the sample. The fourth image is an overlap of all three for comparison purposes.

X-Ray Fluorescence Microscopy

XFM is the process of using a powerful, concentrated X-Ray beam to disrupt the electron shells around atoms. The radiation pushes an electron out of inner shell so an electron from an outer shell has to move in to take its place. This causes a change in energy levels which leads to the emission of radiation and colorful light which is unique to specific elements. This emission can then be quantified and analyzed to determine the concentrations of various elements and ions in the sample.

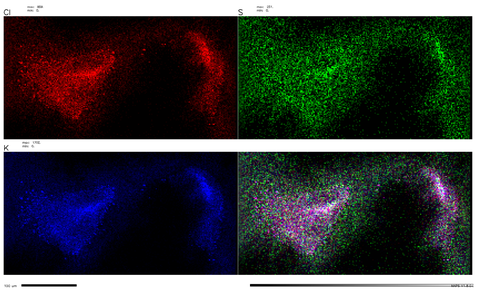


Figure 5 shows a hot spot near the Organ of Corti and highlights chlorine, sulfur and potassium concentrations of which potassium is significant to auditory function and provides information related to the Potassium Recycling Theory of the inner ear.

Conclusions/Future

- Correlation between treatment with *Honokiol* and prevention of hearing loss, especially in younger mice
- Significance of zinc concentrations in bone development
- Hot spots of potassium related to the Potassium Recycling Theory
- Continue XFM's of treated mice cochlea to make more specific conclusions related to cisplatin and *Honokiol*
- Continue using XFM's to understand the auditory system in mice and apply it to humans
- Explore the XFM process to determine more information about samples in future studies
- Use hearing tests with XFM scans to determine correlations and trends in study.

I would like to thank Dr. Claus-Peter Richter and Dr. Xioadong Tan for their guidance throughout this investigation and the Illinois Math and Science Academy for giving me this opportunity.

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