

## **Mitochondrial toxicity of antibiotics in inner ear-derived cultured murine cells**

Johannes Ehinger<sup>1,2</sup>, Tianshi Liu<sup>1</sup>, Eskil Elmér<sup>1,2</sup>, Fredrik Sjövall<sup>1,2</sup>, Imen Chamka<sup>1</sup>

<sup>1</sup> Lunds Universitet, <sup>2</sup> Skånes Universitetssjukhus

**Background:** Ototoxicity is a well-known side-effects of certain classes of antibiotics. It is most well-described for aminoglycosides but has also been reported for e.g. macrolides and vancomycin. Mitochondrial dysfunction is strongly implicated in the pathogenic mechanism at least for aminoglycoside-induced ototoxicity.

**Material and Methods:** Here we investigate the effects of several classes of antibiotic (ciprofloxacin, gentamycin, linezolid, meropenem, and vancomycin) used in intensive care on mitochondrial respiration (oxygen consumption measured with an Oroboros O2K), inner membrane potential (flow cytometry with the probe TMRM), ATP-levels (MgG) and reactive oxygen species formation (ROS, MitoSox and DHE) in the murine inner-ear derived cell line HEI-OC1, after 24 h incubation at dosing correlating to high clinical exposure. Human peripheral blood mononuclear cells (PBMCs) were used as a control cell system.

**Results:** In HEI-OC1 cells, impairment of one or more measures of mitochondrial respiration was seen for all antibiotics tested, most consistently for Vancomycin and meropenem. Levels of ROS were increased for all antibiotics except Vancomycin as measured both with DHE and MitoSox. ATP levels were decreased for gentamycin, linezolid and meropenem. Mitochondrial membrane potential was decreased for Ciprofloxacin and gentamycin. In contrast, no differences in any mitochondrial measure was altered in the WBC for any antibiotic.

**Conclusion:** Mitochondrial function in inner ear-derived cells are sensitive to a wide range of antibiotics in clinically relevant doses, both in terms of oxygen consumption, ROS, production, ATP levels and mitochondrial membrane potentials. This contrasts with PBMCs where no effects were seen.