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In vitro gentamicin exposure alters caveolae protein profile in cochlear spiral ligament pericytes

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Introduction: We have investigated the changes in the protein profile associated with caveolae in gentamicin (GTM) treated and untreated spiral ligament (SL) pericytes. The ototoxic drug GTM is used experimentally to investigate cochlear damage; SL pericytes are specialized cells in the blood labyrinth barrier of the inner ear microvasculature; caveolae, are protein and cholesterol-rich cellular microdomains, which transport small molecules in and out the cells. A different protein profile in transport-specialized caveolae may induce pathological changes affecting the integrity of the blood labyrinth barrier and ultimately contributing to hearing loss.

Method: Caveolae isolation is achieved through ultracentrifugation of the cells lysates in discontinuous gradients. Mass spectrometry (LC-MS/MS) analysis identifies the proteins in the treated and untreated groups. Proteins segregating with caveolae isolated from untreated SL pericytes are then compared to caveolae isolated from GTM-treated SL pericytes. Data are analyzed using bioinformatics tools.

Results: The caveolae proteome in GTM treated cells shows that 40% of total proteins are uniquely associated with caveolae and 15% of the proteins normally associated with caveolae are suppressed. Bioinformatics analysis in GTM treated cells shows a decreased protein expression in genetic information processing. Proteins expression increases in metabolism, vesicular transport and signal transduction processes. Several Rab GTPases are significantly enriched in GTM treated cells.

Conclusion: GTM exposure modifies protein profile of caveolae from SL pericytes. We identified a pool of proteins which are uniquely segregating with caveolae during the treatment, mainly participating in metabolic and biosynthetic pathways, in transport pathways and in genetic information processing.

Biography

Elisa Ghelfi obtained her PhD at the University of Pavia (Italy) with the experimental work on free radicals and lipid peroxidation developed at the Tokyo University Research Center of Advanced Science and Technology (RCAST) (Japan). She is Research Associate at the Harvard T H Chan School of Public Health (USA). She as an extensive scientific work covering the impact of air pollution on the cardiopulmonary physiology; assessing the angiogenesis in bonchial and retinal rmicrovasculatures in hyperoxic/hypoxic conditions; investigating the proteomic of the cocchlea microvasculature subjected to noise and ototoxic drugs. Her research work has received close to 700 citations.

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