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The glutathione conundrum: Stoichiometric disconnect between formation and oxidative stress

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Increased glutamine uptake is known to drive cancer cell proliferation, making tumor cells glutamine-dependent. Studying lymph node aspirates containing malignant lung tumor cells showed a strong correlation between glutamine consumption and glutathione excretion. Subsequent validation in A549 and H460 lung tumor cell lines show that glutamine drives synthesis and excretion of μ molar amounts of glutathione. Glutathione is the most abundant and most widely studied endogenous antioxidant. Glutathione concentrations in normal tissues are in the μmolar range, which is 10,000 fold higher than the concentration of reactive oxygen species. This stoichiometric disconnect has been poorly understood. To understand the molecular function of μ molar concentrations of glutathione in lung tumor model we studied glutathione metabolism. Glutathione is degraded by γ-glutamyl transpeptidase (GGT) by transferring the glutamyl group to amino acids to facilitate the amino acid uptake. Inhibition of glutaminase or GGT essentially abolished glutathione synthesis and formation of γ-glutamyl amino acids. Both enzymes were found to be essential for cell proliferation. Quantitative evaluation of glutathione's many functions led us to believe that glutathione's main function is to store building blocks for biosynthesis and trigger cell proliferation or apoptosis, depending on nutrition availability. Consequently, cell viability is mainly controlled by a stable metabolite, glutathione, instead of the common belief that these processes are controlled by unstable radical chemistry.

Biography

Gunnar Boysen has completed MS Biology in 1996 at the University of Kaiserslautern, The German Cancer Research Center, Heidelberg, Germany. He completed his PhD (Chemistry), Department of Chemistry, University of Kaiserslautern Germany, and University of Minnesota Cancer Center, Minneapolis, MN in 2002. Then in 2005, he completed Postdoctoral studies in the Department of Environmental Sciences and Engineering at The University of North Carolina at Chapel Hill. He is currently Associate Professor in the Department of Environmental and Occupational Health at University of Arkansas for Medical Science, USA.

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