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### Magnesium (Mg) deficiency worsens and Mg replacement protects against cisplatin-induced kidney injury in non-tumor and tumor-bearing mice

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Cisplatin is a potent chemotherapy for treating ovarian and other cancers. Cisplatin-induced acute kidney injury (AKI) occurs in ~25% of patients while hypomagnesemia occurs in 90% of patients. Previous studies have implicated magnesium (Mg) status in cisplatin-induced AKI. We explored the effect of Mg deficiency (MgD) ( $\pm$ Mg supplementation, MgS) in a mouse model of cisplatin-induced AKI. In addition, using an ovarian (A2780) tumor xenograft model, we examined the effect of Mg status on cisplatin-induced AKI and the anti-tumor efficacy of cisplatin. In both non-tumor- and tumor-bearing mice, Mg deficiency (MgD) significantly worsened cisplatin-induced AKI (based on BUN, inflammation, apoptosis and histological scores) while MgS significantly protected against cisplatin-induced AKI. Tumor growth was inhibited by cisplatin and further inhibited by MgS on day 22. MgD did not affect tumor growth or cisplatin-mediating tumor killing. Ongoing studies are exploring the role of Mg status in tumor growth and cisplatin-induced AKI in additional tumor models in mice. In summary, MgD worsens and MgS protects against cisplatin-induced AKI as evidenced by improved kidney function and reduced renal inflammation and apoptosis. While improving kidney function, MgS also improved cisplatin-induced tumor killing. Mechanistic studies reveal that MgD increases renal platinum accumulation through regulating cisplatin transporter expression/function in the kidneys; these effects are not observed in the tumor. These findings warrant future large scale studies to assess Mg status and aggressive Mg replacement therapy in cisplatin-treated patients. In addition, assessment of dose, formulation and timing/duration of Mg replacement in cisplatin-treated patients should be considered to promote renoprotection.

#### Biography

Christine N Metz has completed her PhD at New York University and Post-doctoral studies from New York University and the Picower Institute. Currently, she is the Head of the Laboratory of Medicinal Biochemistry at the Feinstein Institute for Medical Research and Professor in the Department of Molecular Medicine at the Hofstra-North Shore-LIJ School of Medicine. She has been working in the field of inflammation for the past twenty years. She has published more than 125 papers in peer-reviewed and reputed journals. She also holds 5 patents related to her work and has served as an Editorial Reviewer for numerous journals.

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