Cadmium and Other Metals Ions Lack Endocrine Disrupting Activity in Yeast and Mammalian Reporter Assays

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Abstract

Previous reports suggest that cadmium and other metal ions may act directly or indirectly to alter steroid hormone receptor signaling. Here, recombinant yeast engineered to express human androgen, estrogen α or β, glucocorticoid, mineralocorticoid, or progesterone receptors and relevant lacZ reporter genes were used to survey Cd⁺² and other metal ions (iron, mercury, lead, copper, arsenic) for endocrine disrupting activity. No agonist activity for any of the six steroid hormone receptors was detected across broad ranges of metal concentrations. Each receptor-bearing yeast strain was then activated with cognate steroid hormone in a second series of experiments and a range of metal concentrations was used to assess signaling inhibition. Metal ions caused signaling inhibition, but only at concentrations that were near or within the range that also retarded growth or killed cells. Thus, inhibition of steroid hormone receptor signaling by metal ions probably resulted from general rather than selective toxicity of the metal ions. Assessment of metal ion-induced activation of estrogen receptor α signaling was conducted in a recombinant breast cancer cell line with an ERE-directed luciferase reporter gene. As observed in the yeast system, no evidence for estrogenic activity of any of these metal salts was found. Our results clearly show that metal ions (e.g. Cd⁺²) are not simple activators of steroid hormone receptor signaling, and are only inhibitory at generally toxic doses. This project is supported by NIH/NCI R33 CA101622.