MOLECULAR ENGINEERING TITANODRUGS IN CELL DIFFERENTIATION BYPASSING INSULIN RESISTANCE AND INFLUENCING OSTEOGENESIS.

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ABSTRACT

Plethorically dispersed throughout the globe, syndromes and organ dysfunctions have been recognized among symptomatic physiology aberrations, involving metabolic pathologies and Diabetes mellitus II [1]. Therapeutic administration, however, through traditional drugs has been marred by severe side-effects, thereby necessitating development of alternative drugs exhibiting lower toxicity and higher specificity. Consequently, the broader scientific community has turned to the development of new drugs bearing metal ions coordinated to select organic substrates so as to effect solubility-availability and finally specificity. Prominent such choices include vanadium, zinc and chromium drugs among others [2].

Driven by the strict criteria guiding potential metallodrugs into zero toxicity and high specificity, we have launched an investigation into Ti(IV), being isoelectronic to V(V), a species known to exhibit influence on glucose catabolism. Thus, we synthesized Ti(IV) complexes bearing organic substrates originating in the Krebs cycle (e.g. citric acid). The holistically characterized structural speciation of binary T(IV)-hydroxycarboxylato species (in the solid state and solution) facilitated further inquiry into the ability of the complex species to differentiate primary fibroblasts into mature adipocytes , thus expediting glucose uptake and catabolism. The ensuing in vitro biotoxicity profile (3T3-L1 cells) (viability, chemotacticity, proliferation, etc.) served as a screening tool to select species for further biological assessment. Cell differentiation of premature fibroblasts to mature adipocytes was pursued, with atoxic titanoforms showing concentration- and time-dependent cell-differentiating induction under defined conditions. Further molecular biology work revealed gene-specific alterations involved in early cell differentiation events, leading to competent mature adipocytes. Cognizant of the intimate association of adipocyte differentiation to osteogenesis, in-depth perusal of the mileralization-osteogenic potential of the select Ti(IV) species was pursued in parallel (KS483 cells). The results portray vividly the structural features of the Ti(V)-organic assemblies avidly affecting the process, thus justifying the observed osteogenic activity [3]. The collective results denote the importance of Ti(IV)-hydroxycaboxylato complex assemblies in effecting adipocyte cell differentiation counteracting hyperglycemia while promoting osteogenic activity in a bimodal fashion. The so arisen biomaterials give credence to the notion that molecular bioengineering provides appropriately configured titanodrugs as potential therapeutics in Diabetes mellitus II and osteogenic effectors, thus meriting further development of smart pharmaceuticals.

KEYWORDS: Titanium, hydroxycarboxylic substrates, diabetes, cell differentiation, osteogenesis

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