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Development of agonists for the prevention of obesity and obesity-related diseases

R. Stephen Lloyd, Ph.D., Professor, Oregon Institute of Occupational Health Sciences, Department of Molecular and Medical Genetics

The prevalence of human obesity continues to rise, with one-third of all U.S. adults classified as obese, and another one-third overweight. Ramifications of this growing trend are not limited to reduced quality of life and/or self-image, since obesity is highly correlated with comorbidities in a variety of other major secondary medical conditions including elevated heart disease, stroke, type 2 diabetes, fatty liver disease, chronic inflammation, and certain types of cancer. These medical conditions have enormous financial impacts on healthcare and insurance costs that are associated with the treatment and ongoing care for these individuals. Although this epidemic must be first addressed through education concerning the benefits of exercise, balanced diet, and adequate sleep, there are numerous circumstances in which weight gain is highly anticipated as a result of disease progression or pharmacologic treatment. Treatment of such patient populations represents large financial markets in which prevention of weight gain is a win-win-win situation for the patient, healthcare provider and insurance providers. To meet these challenges, our research has identified a mechanism through which diet- or genetic-induced weight gain can be largely prevented by enhancing a normal cellular activity. We propose to translate our findings into pharmacologically tractable approaches, expanding the core structure of our current lead drugs and testing their biochemical/cellular efficacies to enhance this activity. Thus, our goals are to optimize the structure of drug-like molecules that have been selected for enhanced catalytic activity.