Tohoku Univ. Technology

1,3-Dioxolane derivative, D-532

Renal functions and tissues in diabetic nephropaty models is improved through D-532 oral administration.

Fig.1 D-532 and its dose-dependent effects in ChREBP reporter assay

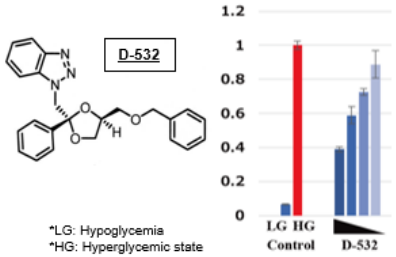
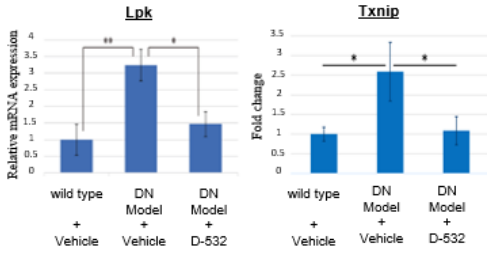


Fig.2 Suppression of ChREBP target genes expression in kidney in DN models with D-532 oral Administration



Overview

The number of dialysis patients continues to increase, and it is known that applox. 40% of the patients requiring dialysis in Japan were ordinally those with diabetic nephropathy (DN). The treatment for DN is often symptomatic by controling blood sugar and blood pressure, and to date, no effective therapeutic agent for curative treatment has been developed.

This invention discloses a 1, 3-dioxolane compounds D-532 and the derivertives thereof, which inhibits the function of the glucose-responsive transcription factor ChREBP (Carbohydrate responsive element binding protein), for DN treatment.

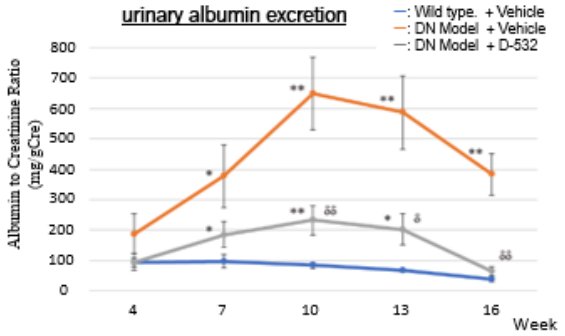
D-532 was found by ordinally constructed high-throughput screening based on ChREBP reporter assay with applox. 7,000 of compound library in Tohoku University (Fig.1). Synthesized analogs and isomers thereof were also tested and showed inhibitory effect against ChREBP function, although D-532 showed the highest activity (Data not shown).

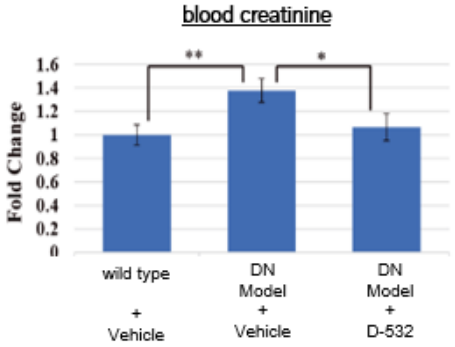
The expression of ChREBP target genes were suppressed by D-532 administration for DN animal model (Fig.2). Urinary albumin excretion and blood creatinine were also improved in DN animals with D-532 (Fig.3). Further, the disappearance of foot process in glomerulus, which is often observed in DN kidney, was suppressed (Data not shown), suggesting that D-532 may act directly to renal tissue and show the effects above.

Product Application

- ☐ DN Treatment Drug

Improvement of urinary albumin excretion and blood creatinine





IP Data

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