New compounds for the treatment of Type 2 Diabetes and other diseases by modulation of the enzymatic complex AMPK

CSIC and CIBER have found a family of indol heterocyclic compounds which act as activators of protein kinase AMPK. This enzyme regulates the energy status of the cell. Therefore, these compounds are useful for the treatment of cancer, metabolic and cardiovascular diseases, among others.

Pharmaceutical companies interested in a patent licence are sought.

Compounds that regulate cellular energy metabolism

Serine/Threonine protein kinase activated by adenosine monophosphate (AMPK) is an enzyme involved in energy production processes such as glycolysis, lipid oxidation and gluconeogenesis. Therefore, AMPK is currently considered as a promising therapeutic target for the treatment of metabolic diseases such as type 2 diabetes and obesity.

Since AMPK is also present in the heart, its activation leads to a decrease in cardiac hypertrophy and heart failure risk.

In addition, activation of AMPK reduces the expression of lipogenic enzymes such as fatty acid synthase (FAS) and acetyl CoA carboxylase (ACC) suppressing in this way the proliferation of prostate cancer cells.

Furthermore, the indol derivatives of this invention have been successfully tested and are able to activate AMPK through assays on mammalian Hek293 cells with values similar to those obtained from Phenformin, a well-known activator of AMPK, but at lower doses.

Therefore, these compounds are especially useful for the treatment of diseases where the function of AMPK is relevant as for example, cancer, metabolic and cardiovascular diseases.

Has been estimated that 439 million people will suffer from type 2 diabetes in 2030.

Main applications and advantages

- The compounds are able to induce *in vivo* activation of AMPK enzymatic complex. It has already been demonstrated the anti-diabetogenic effect of AMPK activation.
- Simple synthesis procedure of new indole derivatives.
- Direct activation of AMPK inhibits prostate cancer growth *in vitro* and *in vivo*. Persistent activation of AMPK results in mitotic arrest and apoptosis of prostate cancer cells.
- Inhibition of de novo lipogenesis is the key mechanism of AMPK-mediated anti-tumor effect.

Patent Status

Priority patent application

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