Repurposed Drug for the Treatment of Nephrogenic Diabetes Insipidous

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Technology description

Market Summary

Nephrogenic diabetes insipidus (NDI) is a form of diabetes insipidus due primarily to problems in the kidney, in which the kidney is unable to concentrate urine. It is defined as a rare or orphan indication that impacts approximately 40,000 less individuals annually in the US and about 200,000 world-wide. The vast majority of cases (~90%) are acquired mostly due to chronic lithium use, the remaining 10% being due to hereditary causes. Currently there are no therapies specifically targeted towards treating NDI. Lifestyle modifications such as increased water consumption and changes in diet (reduced salt and protein intake) are the most commonly employed treatments. Diuretics such as amiloride or hydrochlorothiazide can also be used to manage urine output, but do not treat the underlying cause of the disorder.

Technical Summary

An approved drug for the treatment of type II diabetes mellitus, metformin, works by activating AMP-activated protein kinase (AMPK). Dr. Sands and colleagues have recently discovered that administration of metformin to kidney tissue samples from rats and mice activates AMPK and thus causes the phosphorylation of two of the primary proteins involved in the ability to concentrate urine, water channel aquaporin 2 (AQP2) and urea transporter UT-A1. When these proteins are active, more water is retained within the body and less is excreted. During cases of NDI, a sufficient amount of antidiuretic hormone, ADH (vasopressin, AVP) is produced however the kidneys do not respond properly to ADH and are therefore unable to properly concentrate urine by removing water. Emory researchers believe that although both AQP2 and UT-A1 are regulated by ADH, the activation of these proteinsviaAMPK is independent of that mechanism and therefore is a new potential treatment path for NDI. In additionalin vivotests using a mouse model of NDI, they showed that intraperitoneal injection administration of metformin leads to an increase in osmolality of the urine and hence an increase in urine concentration. Based upon these findings, metformin and other AMPK agonists may treat the underlying causes of NDI, as opposed to only the symptoms of the disorder.

Application area

New use for metformin or other AMPK activators in treating nephrogenic diabetes insipidous (NDI).

Advantages

Lead candidate, metformin, is FDA-approved, safe, and currently in use for treating type II diabetes mellitus.
There is no therapeutic available for NDI, current therapies only address symptoms.
Repurposed metformin addresses the underlying cause of NDI.

Institution

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