Use of Riboflavin for the Targeted Treatment of High Blood Pressure

Ulster University research has led to the discovery of a novel gene-nutrient interaction in blood pressure (BP) and the development of a new non-drug therapy for lowering blood pressure in people with a genetic predisposition for developing high blood pressure (BP) (i.e. hypertension).

Background and Technology:

Hypertension is the most common risk of heart disease, responsible for ~62% of stroke and ~49% of coronary heart disease cases. It is estimated that up to 60% (1.56 bn) of the world’s adult population will suffer from hypertension related problems by 2025. Despite the availability of effective anti-hypertensive drugs, hypertension remains uncontrolled in many patients.

One emerging genetic factor of hypertension under investigation is the C677T polymorphism. This gene encodes the folate metabolizing enzyme methylenetetrahydrofolate reductase (MTHFR) and is the main genetic determinant of elevated homocysteine in blood. The homozygous mutant (TT) genotype results in a variant MTHFR enzyme with decreased activity in vivo. Approximately 10% of people worldwide have the MTHFR 677TT genotype, but its frequency is much higher in some populations e.g. Mexico (30%) and Northern China (20%).

Molecular studies demonstrate that the decreased activity of the variant MTHFR enzyme is owing to the loss of its riboflavin (i.e. FAD) cofactor. We have conducted a series of clinical studies testing riboflavin as a novel BP-lowering treatment in targeted patient groups who were pre-screened for the C677T polymorphism. To date, we have published three trials of BP-lowering in response to supplemental riboflavin:

- Horigan et al 2010: an investigation of patients with premature CVD (i.e. had a CVD event below age of 55 years, as per WHO definition of premature CVD);
- Wilson et al 2012: follow-up of above patients four years after the initial investigation;
- Wilson et al 2013: investigation of a separate group of patients with hypertension but no overt CVD.

Despite the majority of participants being treated additionally with routine anti-hypertensive drugs at the time of recruitment and throughout the trials, the BP-lowering effect of riboflavin was shown to be independent of any drugs.

This evidence indicates that riboflavin offers much potential in the area of personalised medicine as an effective option to treat hypertension in genetically at-risk people, possibly combined with an existing anti-hypertensive drug as a novel combination therapy targeted at this specific genetic group.
Benefits:

- A combination product incorporating U104 has the potential to increase efficacy in patients genetically predisposed to hypertension, who are relatively resistant to current antihypertensive treatments.

- Riboflavin is a well-recognised essential B vitamin, with no reported adverse effects even at very high doses (over 100 fold higher than those shown to be effective for BP-lowering in our trials). Time to market and regulatory requirements for combination therapies incorporating riboflavin are therefore much reduced.

- U104 provides the opportunity to develop new formulations combining this novel treatment with existing hypertensive agents coming off patent.

- We offer an option for personalising hypertension treatment through a novel combination therapy targeted at patients sharing this common genetic variant.

- There may also be the scope for developing a new combination drug with a companion diagnostic.

Publications:


Collaborators:

Western Health & Social Care Trust, Northern Ireland

Trinity College, Dublin, Ireland

Patent Status:


Lead Inventors:

- Professor Helene McNulty
- Professor Mary Ward
- Professor Sean Strain

Licensing & Partnering Opportunity:

Ulster University is actively seeking a strategic partner to assist in the further development of its U104 technology providing a route to market for the safe and effective treatment of hypertension.

The University is open to a variety of models for collaboration including sponsored research, out-licensing and co-development. The inventors of this technology are able to provide valuable know-how to assist in its successful commercialization.

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