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Expert Spotlight: Safety studies for drugs affecting blood pressure

Ejaz Ansari is one of REPROCELL's resident experts in human fresh tissue research. He is a leading authority in organ bath and ussing studies, and has contributed to over 200 preclinical projects at REPROCELL.

Ejaz's career began with us more than 13 years ago, when he was a pharmacology graduate . He is now acting Laboratory Manager at our ***Centre for Predictive Drug Discovery*** in Glasgow, UK – the first laboratory in the world to commercialise human fresh tissue research, and the leading human tissue contract research organisation (CRO).

During his time at REPROCELL, Ejaz estimates that he has conducted well over a thousand organ bath experiments using human blood vessels. Through his contributions in designing and conducting circulatory safety studies for a range of compounds he has honed his expertise in blood vessel dissection, pharmacology, and quality assurance.

In his most recent publication, Ejaz helped Alucent Biosciences determine the effect of their peripheral artery disease (PAD) treatment in human tissues. Read on to find out more about his work on this study.

Publications

Retained Functionality of Atherosclerotic Human Arteries Following Photoactivated Linking of the Extracellular Matrix by Natural Vascular Scaffolding Treatment (2020)

Potentiating TMEM16A does not stimulate airway mucus secretion or bronchial and pulmonary arterial smooth muscle contraction (2020)

Expert Spotlight: A light-activated cure for PAD?

Researchers at Alucent Biomedical have developed a light-activated compound which can treat PAD without the need for artificial implants.

Upon exposure to a specific wavelength of light, this small molecule enables cellular proteins, such as collagen and elastin, to link together – forming of a natural vascular scaffold (NVS). We asked the lead-author of the latest study, Ejaz Ansari, about this fascinating novel treatment.

How did you determine that NVS was safe for use in human blood vessels?

Because NVS changes the blood vessel structure, our main concern was that it would affect blood pressure – which could produce dangerous side effects in humans.

Previously, the drug has been tested in porcine blood vessels where it was shown to have no effect on natural blood vessel constriction – but we wanted to be sure. So in this study, we measured constriction in fresh, functional popliteal arteries from human donors.

It is important to note that there are ethical considerations when using tissues from human donors. We had to ensure that all tissues were donated with informed-consent under guidelines provided by the Human Tissue Authority and that patient data was completely anonymised.

> **“As a result of this study’s success, Alucent Biomedical are now trialing NVS in human subjects.”**

What experimental methods did you use?

Our scientists used a tissue bath methodology in this experiment. Popliteal arteries from three coronary vascular disease (CVD) donors were suspended in a tissue bath, pre-treated with NVS and light and exposed to a vasoconstrictor (U46619) and a vasorelaxant (sodium nitroprusside). This allowed us to test whether the drug had a significant effect on normal physiological activity – it did not (Figure 1).

The tissue bath method is an established, but highly specialized pharmacological method for estimating drug effects on blood pressure. We therefore had to ensure that all experiments had adequate controls in place and that tissue viability was confirmed.

What quality control methods were put in place for this work?

Researchers at Alucent Biomedical used histological analysis to confirm the presence of atherosclerotic plaques, changes in extracellular matrix structure, and drug distribution within the donor tissue following treatment. Through this analysis, they confirmed that drug distribution was even, and that treated blood vessels had denser arterial walls than those exposed to the negative control.

One of the experimental outcomes showed that the drug may reduce inflammation – how did you measure this?

Following treatment, we cultured some artery rings in cell culture media and measured the levels of interleukin-6 (IL-6) in the supernatants to check for any drug induced inflammation. ELISA results showed reduced cytokine levels in NVS treated samples suggesting NVS may exert an anti-inflammatory effect.

As a result of this study’s success, Alucent Biomedical are now trialing NSV in human subjects. Their phase one trial will test NVS in 15 patients with symptomatic PAD, using a single group assignment method. It’s a very exciting time for Alucent Biomedical – I wish them every luck with this clinical trial and any future work.