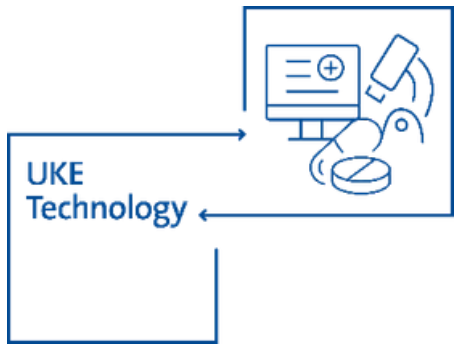

Refining treatment of heart failure
Specific targeting of detrimental ß$_1$-adrenoceptor pool

Background & Innovation

Constantly increasing prevalence of **cardiovascular disease** is a major burden of modern society. Despite huge efforts in drug development, the 5-year mortality from heart failure unfortunately remains 50%, and the treatment costs amount to around €30 billion euros.

It is accepted that **ß$_1$-adrenergic receptors (ß$_1$-AR)** play a major role in the signalling cascade responsible for heart **hypertrophy, dilation and fibrosis**. Therefore, ß-blockers belong to the most frequently prescribed drugs, and a decrease in mortality rates in heart failure has been documented.

However, due to the reduction of cardiac contractility, classical ß-blockers have a limited use after acute myocardial infarction and in severe NYHA-IV heart failure.

We are presenting here a **new generation of more specific ß$_1$-AR-blockers** which do not decrease cardiac contractility and can therefore be used early at the onset of disease and in patients not addressed by available drugs.

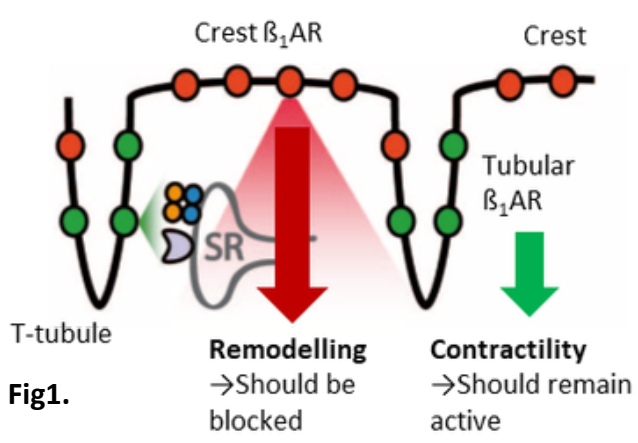

Fig1.

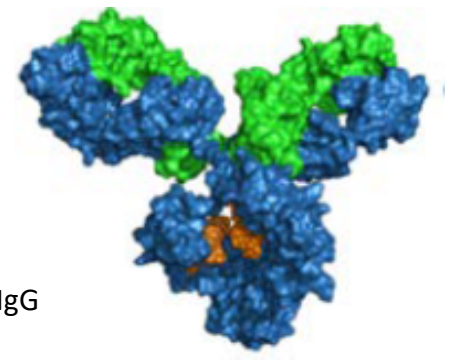

Fig2. Atenolol IgG

Technical Description

The inventors could demonstrate that T-tubular and outer membrane (crest) ß$_1$-AR/cAMP nanodomains differen-tially regulate cardiac contractility and remodelling (see Figure 1). As current ß$_1$-AR-blockers do not differentiate be-tween these structures, the inhibition of **hypertrophy is necessarily linked to the decrease of contractility.**

Our innovative drug candidate is capable of specifically blocking the pool of **ß$_1$-AR located in the cell crest of cardiomyocytes**. These receptors are involved in the undesired cardiac remodeling (i.e. hypertrophy, dilation and fibrosis), but not in cell contrac-tility. In contrast, ß$_1$-ARs which are located in the T-tubules responsible for the regulation of cardiac contrac-tility are not affected by our drug candidate.

This drug candidate comprises an IgG antibody complex covalently linked with a beta blocker to ensure optimal pharmacokinetics (see Figure 2). This patented innovative approach has shown a high **efficacy in vitro and also in vivo (mouse experiments).**

Competitive advantage

Our innovative therapeutic approach presents a highly specific ß$_1$-AR-blocker to enhance the current drug market through clear advantages:

- **Specific targeting of detrimental ß$_1$-AR pool**
- **Inhibition of hypertrophy and cardiac remodelling**
- **Reduced adverse effect on contractility**
- **Significant improvement of patient's quality of life**
- **Can be used after acute myocardial infarction and in severe heart failure cases**

FOCUS SECTORS
- Therapeutics
- Cardiovascular disease
- Active ingredient discovery

PROJECT KEY WORDS
- Heart failure
- ß$_1$-adrenoceptors
- Blocking cardiac remodelling
- Unaffected contractility

DEVELOPMENT STATUS
- In vitro tests
- Langendorff hearts tested
- In vivo tests successful

PATENT PROCEDURE STATUS
- US patent granted
- EU and Canada patent pending

POTENTIAL FOR OOPERATION
- R&D Cooperation
- Transfer of rights
- Licensing

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