COLLABORATION TO TARGET ATRIAL FIBRILLATION

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When the heart begins to beat much faster or in an irregular manner, this can be a sign of atrial fibrillation (AF). Though it doesn’t come with the fanfare associated with diseases like cancer, AF has rapidly become one of the most important public health problems in developed countries. It is due in no small part to its disproportionate effects on the elderly, who are of course growing in numbers thanks to the ageing population in regions like Europe and North America.

AF is not only dangerous – associated with a twofold increase in mortality – it is also strengthening the European biotech/ pharma sector, especially those coming from regions like Europe and the rest of the world.徘

The aims of AFib-TrainNet are ambitious. By the time the project comes to a close, the researchers involved would like to have found novel mechanisms and targets in AF that can be used to develop new medicines that are both safe and efficient. In doing so, they would provide hope for the millions of people in Europe and the rest of the world suffering from AF. However, that is just one part of the project. Equally as important, AFib-TrainNet is investigating two drug targets, both of which have demonstrated electrical properties during atrial arrhythmias: the G-protein inward rectifier potassium current (IK,ACH), and the small conductance calcium-activated potassium current (SK). The students began their work between March and August last year, and according to Jespersen there have been some promising outcomes since then. ‘We have already deciphered a number of cellular mechanisms involved in controlling these two targets. This is important to do first to understand the full involvement of them in the pathogenesis of AF,’ he explains.

What sets the targets chosen for this project apart from previous targets is that they are primarily expressed in the atria of the heart, not the ventricles. This is a crucial detail. One of the reasons the treatments currently in use are so ineffective is that they bring about unwanted side-effects in the ventricles, as they target ion channels that are expressed in both sections of the heart.

With this basic groundwork in place, everyone involved is now working on developing and refining methodologies that will allow them to test their targets in minute detail. These methodologies include ex vivo electrophysiology, human stem cells, and in silico modelling, and thanks to the involvement of the industry partners AFib-TrainNet has at its disposal the very highest of high-tech tools. Acesion Pharma, for example, gives research institutions the chance to access the QPatch, an automated patch clamp robot that the company uses for its medium throughput screening of compounds. More generally, the company provides access to its library of SK inhibitors, as well as its wealth of scientific expertise in the field. While Simô Vicins works at Acesion Pharma exploring how exactly these inhibitors bind to ion channels, these same inhibitors can also be used by the rest of the PhD cohort in order to further their own projects.

MEDICINES OF THE FUTURE

A crucial part of the programme is the creation of a high-quality supervision network with quality assurance measures in place. It is, after all, supposed to be a training programme as well as a means by which to discover new drug targets. Senior researchers and PhD students meet often, and every half year the entire team gets together for an AF training event, which mean the PhD students – a mixed group consisting primarily of women from southern European countries – tend to meet approximately every three months. There is also an intensive exchange schedule, so that all the students get the chance to travel to the different participating partners and experience both industry and academia. All of this, of course, is not just for the personal benefit of those involved. It also means that knowledge is shared and synergies between groups achieved, resulting – hopefully – in better results for the project as a whole.

The European Union has given the go-ahead to the the EU Training Network in Novel Targets and Methods in Atrial Fibrillation (AFib-TrainNet). This programme serves the dual purposes of investigating two potential new drugs targets for atrial fibrillation treatment, and training a group of 15 PhD students, who have the potential to spearhead future research efforts in this field.

The project is being led by Professor Thomas Jespersen at the University of Copenhagen, Denmark, who has high hopes about the potential this project has for developing the student’s capacity as researchers. By partnering with research institutions and industrial partners, the programme promotes an understanding of the whole drug development process. ‘These researchers will thereby have the potential to drive industry/biotech development forward, leading to product development and not only improving life quality and length for many patients but also strengthening the European biotech/ industry sector,’ he enthuses.

Professor Thomas Jespersen leads the Cardiac Physiology Laboratory at the University of Copenhagen, Denmark. He has a PhD in molecular biology from the University of Aarhus, Denmark, and has worked as a postdoctoral researcher at the University of Lausanne, Switzerland, and the University of Copenhagen.

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Impact Objectives

- Provide high quality interdisciplinary research and industry training to 15 international PhD students
- Investigate the potential of two novel drug targets for treatment of atrial fibrillation

Training the next generation

A project led by Professor Thomas Jespersen is training early stage researchers in the field of atrial fibrillation. We talked to him and Rafel Simó Vicens, one of the PhD students benefiting from the programme at Acesion Pharma.

To begin, what is atrial fibrillation (AF) and why does it require the attention of Europe’s biomedical research community?

TJ: AF, a complex and multifactorial disease and the most common sustained cardiac arrhythmia, occurs in 1-2 per cent of the population. More than 6 million Europeans suffer from this arrhythmia and its prevalence will more than double in Europe during the next 40 years due to increased life expectancy. AF has assumed epidemic proportions.

What are your backgrounds, and what led to your interest in your respective fields?

TJ: After my PhD in molecular biology I changed gear and started a postdoctoral research position at the University of Copenhagen, Denmark, in cellular electrophysiology. During a three year postdoctoral period in Lausanne I started working with cellular aspects of cardiac electrophysiology. After coming back to the University of Copenhagen I complemented those technologies with work on cardiac tissue and functional isolated hearts, primarily focusing on cardiac arrhythmias.

RSV: I studied pharmacy at the University of Barcelona, Spain, and specialised in pharmaceutical research and industry. During my studies in Barcelona I worked in pharmacies, hospitals and research laboratories across Europe. Although in Spain pharmacists tend to end up working in community pharmacies and hospitals, I decided to pursue a career in research and industry, specifically in drug discovery and development.

How did you initially become involved in the EU Training Network in Novel Targets and Methods in Atrial Fibrillation (AFib-TrainNet), and what appealed to you about it?

RSV: I came across the AFib-TrainNet project and the list of PhD positions that were offered within the programme. Among all the interesting projects, there was one that immediately caught my attention. The position was offered by Acesion Pharma, a young Danish pharmaceutical start-up company developing new drugs to treat AF, located in Copenhagen. The project included an exciting programme in drug discovery and development, combining pharmacology, molecular biology, drug screening and electrophysiology and represented a unique chance to work in both industrial and academic research. Moreover, and in contrast with big pharmaceutical companies, it offered me the chance to be part of every phase in a drug development programme, from the early drug discovery to lead optimisation followed by the preclinical and clinical assays. Also, the opportunity to work in a dynamic and international network including some of the most renowned institutions and the access to their expertise made this a very attractive position.

Therefore, I decided to apply for this PhD and, luckily, I was selected for the job.

TJ: This European Training Network (ETN) programme is a highly interesting modality to establish a European network built on excellent science and high impact training of PhD students, also bridging to industry. For the involved researchers/biotech companies it fulfilled the wishes we had for funding a research collaboration around discovering and evaluating novel target for AF treatment. Further, a positive evaluation of an ETN application demands profound involvement of industry – which was exactly what we already had in pipeline.

Why is there a need for a project that trains PhD students in the context of investigating novel drug targets?

RSV: Over the past years, a number of drugs have been developed for rhythm control therapy and treatment of AF. Unfortunately, these drugs are only moderately effective and have many adverse effects. Therefore, it is important to find new atrial selective targets for AF treatment and understand the pathological mechanisms.

The creation of an international network with highly skilled professionals and future researchers can improve the communication between institutions and increase the dynamics of the field. Furthermore, these projects not only encourage, but demand that both public institutions and private companies are included in the same network, making it easier to share their knowledge and offer their expertise in a bilateral, open and transparent way.