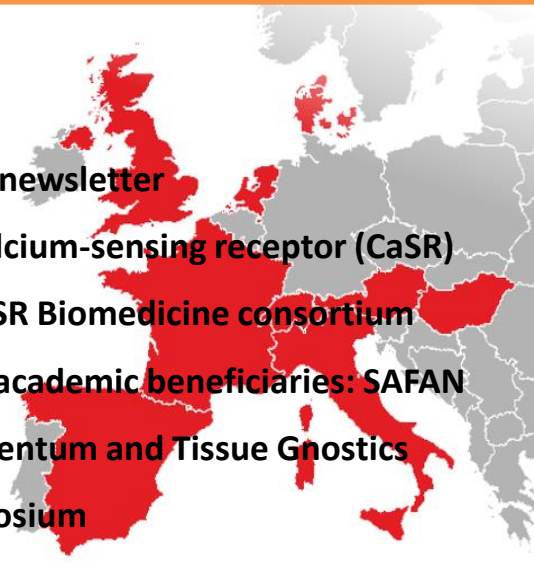


**IN THIS ISSUE:**

- ❖ Introduction to the newsletter
- ❖ Relevance of the calcium-sensing receptor (CaSR)
- ❖ Overview of the CaSR Biomedicine consortium
- ❖ Profiles of the non-academic beneficiaries: SAFAN Bioinformatics, Biotalentum and Tissue Gnostics
- ❖ Events - CaSR symposium



This issue focuses on the role of the non-academic Beneficiaries, S.A.F.A.N. , BioTalentum Ltd. and TissueGnostics GmbH

**Introduction to the newsletter**

The CaSR Biomedicine newsletter will be issued periodically to provide updates on the latest achievements of this Marie Curie Actions European Training Network (ETN), and to provide a forum for the wider community of researchers engaged in the study of the calcium-sensing receptor biology, as well as in calcium and bone metabolism research.

**Relevance of the calcium-sensing receptor (CaSR)**

Abnormal CaSR function or expression contributes to the pathogenesis of major non-communicable diseases that account for >25% of the global disease burden. The scientific goals of the CaSR Biomedicine network are to elucidate ligand- and tissue-dependent differences in CaSR physiology by examining its signalling and function at the cellular level; to assess how CaSR function is altered in Alzheimer's Disease (AD), chronic pro-inflammatory airway disease, diabetes mellitus (DM), sarcopaenia, and cancer, which represent leading causes of morbidity and mortality in Europe; and to develop CaSR-based therapeutic approaches for these major age-related disorders.

**Overview of the CaSR Biomedicine Consortium**

The CaSR Biomedicine European Training Network (ETN) is a fully translational project that utilises a single molecule, the calcium-sensing receptor (CaSR), which influences a range of physiological and disease processes, to develop a unique, strong multidisciplinary and intersectoral scientific training programme, training 14 young scientists to become specialists in G protein-coupled receptor biology and signalling.

This European Network formed of 13 research groups from eight countries will undertake a systems biology approach to study the importance of cellular context in the functionality of the same molecule, the CaSR, across different tissues (e.g. lung, pancreas, gastrointestinal tract) and pathologies (asthma, diabetes, Alzheimer's disease, sarcopaenia, cancer) to identify novel therapeutic approaches of CaSR-targeting drugs that could be repurposed for the management of these major diseases.



The University of Manchester



## Overview of the CaSR Biomedicine consortium

### Coordination Team



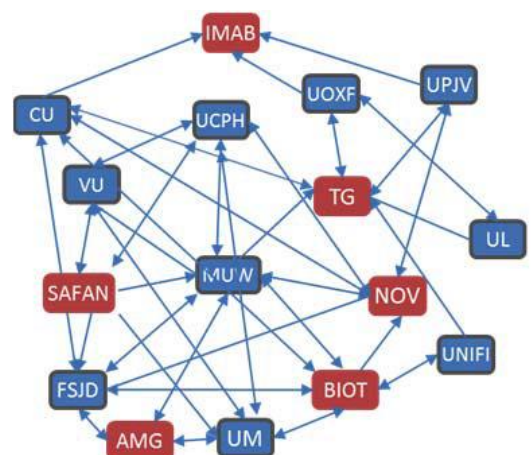
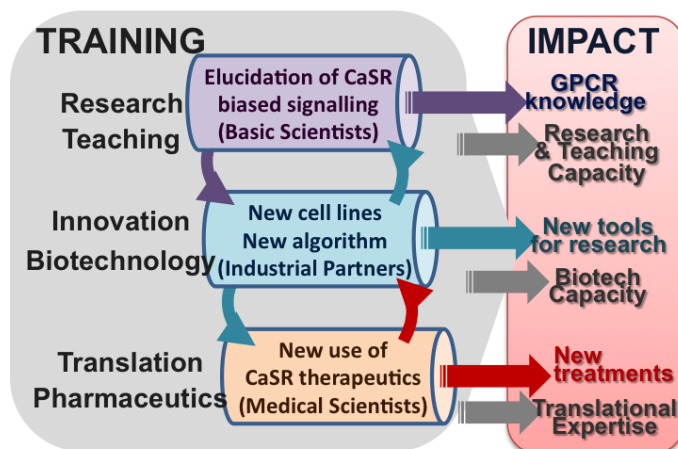
This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 675228.

### Beneficiaries



Academic and non-academic beneficiaries, partner organisations and the advisory board members during the Kick-off meeting in April 2016 at TissueGnostics Headquarters, Vienna. Learn more about the non-academic beneficiaries in CaSR Biomedicine on the following pages.

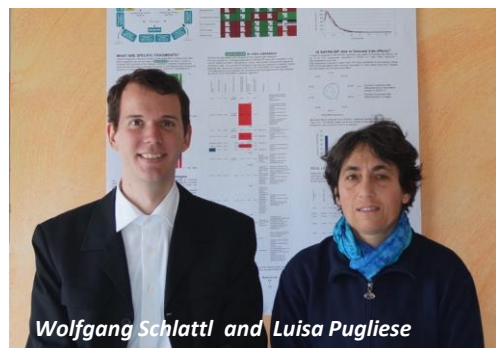
### Project



## Profiles of non-academic beneficiaries

### S.A.F.A.N. Bioinformatics; PI: Dr. Luisa Pugliese

S.A.F.A.N BIOINFORMATICS was founded in 2004 by Dr. Luisa Pugliese, and is a privately funded company specializing in structural bioinformatics. S.A.F.A.N has a particular focus on small molecule *in silico* profiling by fragment informatics and machine learning approaches.



#### Individual ETN research project

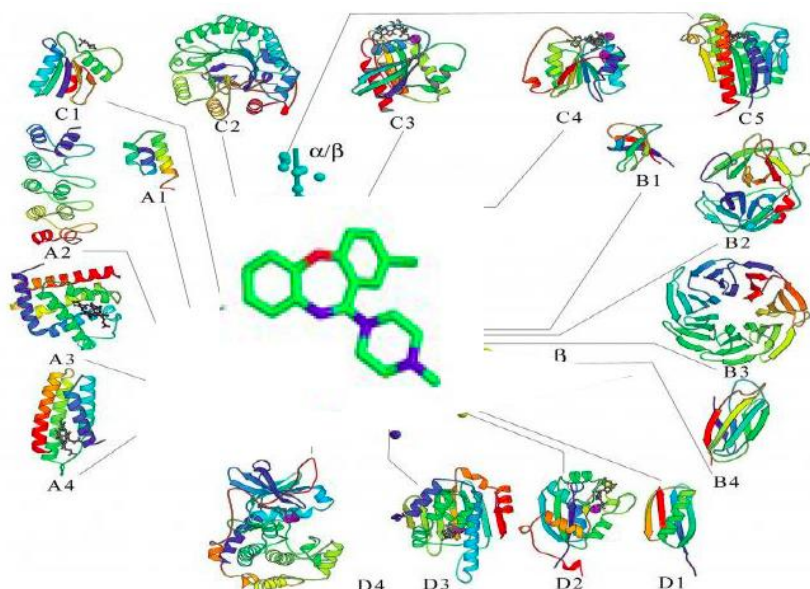
##### *In silico* analysis of CaSR-ligand interactions

Wolfgang Schlattl (ESR)

The aim of this study is to identify and evaluate the ligand specificity of CaSR modulators. In particular, small molecule libraries will be profiled *in silico*, and a homology model of the CaSR will be generated so that the molecular docking of compounds identified from *in silico* profiling can be analysed. Molecular dynamic simulation techniques will also be used to characterise the dynamic behaviours of the CaSR and of the complexes resulting from molecular docking experiments.

#### Wolfgang:

"I am excited to participate in a CaSR drug repositioning project by applying structural biology techniques."



SAFAN-ISP: Profiling: One small molecules  $\rightarrow$  Thousands of targets



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**SAFAN-ISP:** Drug repurposing is widely performed by specific computational technologies. S.A.F.A.N BIOINFORMATICS developed SAFAN-ISP, an *in silico* approach for drug repositioning outperforming most of the other methods available. We are excited to apply it to find repurposing opportunities for CaSR receptor modulation.

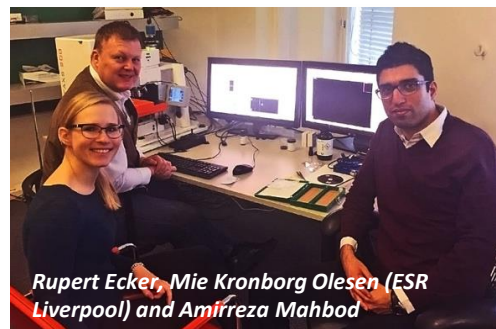
## Profiles of non-academic beneficiaries



TissueGnostics

### TissueGnostics GmbH; PI: Dr. Rupert Ecker

TissueGnostics (TG) is an Austrian company that uses versatile automated microscopy systems for high content and/or high throughput scanning and analysis of biomedical, veterinary, natural sciences and technical microscopy samples. TG has been founded by scientists from the Vienna University Hospital (AKH) in 2003. It is now a globally active company with subsidiaries in the EU, the USA and China and customers in 28 countries.



Rupert Ecker, Mie Kronborg Olesen (ESR Liverpool) and Amirreza Mahbod

#### Individual ETN research project

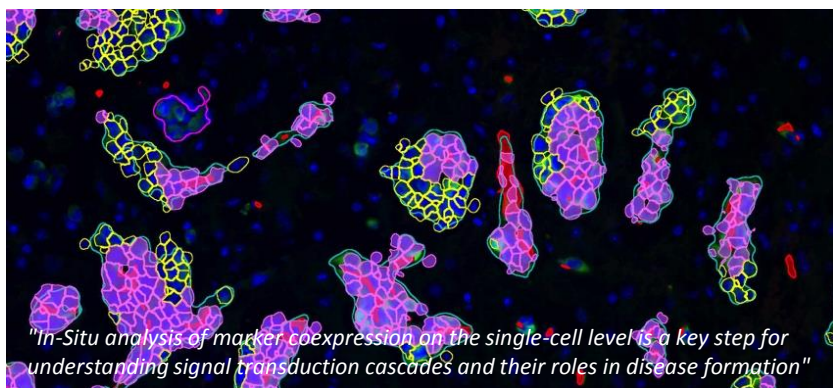
*Generation, validation and application of algorithms for tissue segmentation used in advanced tissue cytometry, Amirreza Mahbod (ESR)*

The aim of this study is to generate segmentation algorithms so that automated image cytometry can be used to characterise a range of cells and tissues, which include parathyroid glands, pancreatic islets, colon tumours and vascular endothelial cells. These algorithms will enable identification and quantitative measurement of cell and tissue characteristics such as cell number & size, tissue area, cell-cell distances, and cellular/sub-cellular localisation.

**Amirreza:** "Segmentation and classification of microscopic images in real world settings is a very interesting research topic for me. Working in the CaSR Biomedicine project and at TissueGnostics GmbH, I have the opportunity to investigate state-of-the-art algorithms, focusing on deep neural networks for their use on histology samples."

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<http://www.tissuegnostics.com>



"In-Situ analysis of marker coexpression on the single-cell level is a key step for understanding signal transduction cascades and their roles in disease formation"



Rupert Ecker welcomes the team at TissueGnostics headquarters, Vienna

#### Applications of TG-products – relevant publications:

A mouse model to identify cooperating signaling pathways in cancer. Musteanu M, Blaas L, Zenz R, Svinka J, Hoffmann T, Grabner B, Schramek D, Kantner HP, Müller M, Kolbe T, Rüllicke T, Moriggl R, Kenner L, Stoiber D, Penninger JM, Popper H, Casanova E, Eferl R. *Nat Methods*. 2012 Sep;9(9):897-900.

Toll-Like Receptor 4 Is Essential in the Development of Abdominal Aortic Aneurysm. Lai CH, Wang KC, Lee FT, Tsai HW, Ma CY, Cheng TL, Chang BI, Yang YJ, Shi GY, Wu HL. *PLoS One*. 2016 Jan 7;11(1):e0146565.

## Profiles of non-academic beneficiaries



### BioTalentum; PI: Prof. Dr. András Dinnyés

BioTalentum Ltd is an RTD research intensive SME, a leading technology provider in Central & Eastern Europe, working on stem cell research and services. Our scientific focus is on medical and animal biotechnologies, specialized on stem cell research. The company's mission is research and development of novel human cellular systems and animal models for biomedical research and drug testing, and to provide technical services for research teams and the pharmaceutical industry.



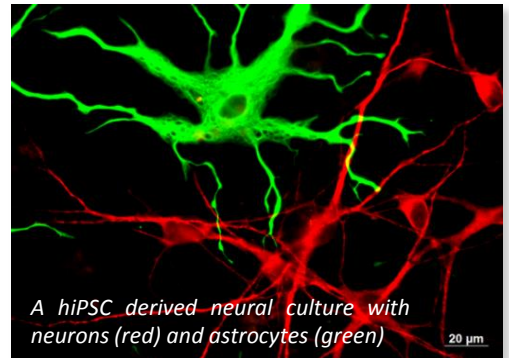
András Dinnyés and his team

#### Individual ETN research project

*Role of CaSR in the pathomechanisms of Alzheimer's disease*  
*Maria Lo Giudice (ESR)*

Alzheimer's disease (AD) affects nearly 30 million people worldwide, and is caused by amyloid-beta induced central nervous system cell loss. According to a hypothesis, amyloid-beta activates the CaSR, inducing intracellular responses in neurons and astrocytes which exacerbate the brain's pathological conditions. Thus, blockers of the CaSR could be used to prevent amyloid-beta toxicity. To identify the role of CaSR in AD, we will develop human induced pluripotent stem cells (hiPSC) derived neuronal cell cultures from AD patients and healthy controls. We will determine CaSR expression and signalling, and investigate whether blocking the receptor will normalise the AD-related *in vitro* phenotypes.

**Maria:** "I have been interested in the brain since I was a child. Studying the iPSC derived neurons represents a unique opportunity to understand better how the brain works and how it is damaged by Alzheimer's Disease."



A hiPSC derived neural culture with neurons (red) and astrocytes (green) 20 µm

#### Relevant publications:

Chandrasekaran A, Avci HX, Leist M, Kobolák J, Dinnyés A. Astrocyte Differentiation of Human Pluripotent Stem Cells: New Tools for Neurological Disorder Research. *Front Cell Neurosci.* 2016 Sep 26;10:215.

Zhou S, Szczesna K, Ochalek A, Kobolák J, Varga E, Nemes C, Chandrasekaran A, Rasmussen M, Cirera S, Hyttel P, Dinnyés A, Freude KK, Avci HX. Neurosphere Based Differentiation of Human iPSC Improves Astrocyte Differentiation. *Stem Cells Int.* 2016;2016:4937689. doi: 10.1155/2016/4937689.

Zhou S, Ochalek A, Szczesna K, Avci HX, Kobolák J, Varga E, Rasmussen M, HolstB, Cirera S, Hyttel P, Freude KK, Dinnyés A. The positional identity of iPSC-derived neural progenitor cells along the anterior-posterior axis is controlled in a dosage-dependent manner by bFGF and EGF. *Differentiation.* 2016 Oct - Nov;92(4):183-194.

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[info@bitalentum.hu](mailto:info@bitalentum.hu)  
<http://www.bitalentum.eu>



The Agricultural Biotechnology Institute in Gödöllő, Hu., where the BioTalentum laboratories are located

## Events

1<sup>st</sup> Annual meeting and ETN School of the CaSR Biomedicine Consortium  
Somerville College, Oxford, 12-16<sup>th</sup> December 2016

**Eliana Goncalves Alves**  
(ESRs' Representative):

*The 1<sup>st</sup> ETN School was held in Somerville College and was a great opportunity for the new ESRs from the CaSR Biomedicine Training Network to get to know each other and all the members of this consortium. During this week there was not only time for the ESRs to absorb all the knowledge and advice given by their principal investigators and the advisory board members, but also to strengthen the relationship among each other. During the 1<sup>st</sup> Annual Meeting (the last two days of this week) there was the chance for the ESRs to present their plans and any initial data that they may have. There was lively discussion being held as well as good input from all the attendants. In my personal opinion there seems to be a bright future ahead for the research of the calcium-sensing receptor. "*



Eliana Goncalves Alves



ESRs during the 1<sup>st</sup> ETN school



Gala dinner at Somerville College



The ESRs, their supervisors and the members of the advisory board



Host Prof. Rajesh Thakker

## Forthcoming event



**3<sup>rd</sup> International Symposium on:  
The Calcium-Sensing Receptor (CaSR)**

**Florence (Italy), May 11<sup>th</sup> – 13<sup>th</sup>, 2017**

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