HIGHLIGHT: A PROFESSOR SOARS TO NEW HEIGHTS
Professor Sai Reddy’s career reached a new peak with his appointment as Associate Professor at ETH Zurich in July 2018. The success story of this professorship at the Basel-based ETH Department of Biosystems is largely due to the generous donation of the Misrock Foundation. On behalf of ETH Zurich and the recipient, we would like to thank the Misrock Foundation most sincerely for its many years of loyal support.

The appointment as Associate Professor coincides well with a new phase in Sai Reddy’s professorship: after six years of establishing his group and developing new methods, Professor Reddy will now concentrate on translating research results into clinical applications, including possibilities for commercialisation. A particular focus of interest and growing activity is cancer immunotherapy.

Sai Reddy investigates the molecular and genetic basis of the immune system and has been instrumental in shaping the emerging field of systems immunology. A central area of research in this new field is the combination of high-throughput experimental techniques, computational biology and big data analysis. Professor Reddy is also helping to define the exciting new area of synthetic immunology, which aims to reprogramme immune cells using advances in genome engineering. His research results open up unprecedented possibilities for the development of personalised and precision vaccines and immunotherapies.
From one highlight to the other: as announced in December, Professor Sai Reddy has been appointed Vice Director of the Botnar Research Centre for Child Health (BRCCH) in Basel. Together with the founding director Professor Georg Holländer, who holds a dual professorship in pediatric immunology at the universities of Basel and Oxford, he will now head the BRCCH.

Botnar Research Centre for Child Health (BRCCH) in Basel

Supported by the generous contribution of the Swiss Fondation Botnar in Basel, the University of Basel and ETH Zurich co-founded the Botnar Research Centre for Child Health (BRCCH) on 19 September 2018. The centre seeks to generate tangible results in pediatrics to help prevent diseases, develop new treatment approaches, improve diagnoses and effectiveness forecasts, and make healthcare systems more affordable. To do so, it combines the expertise of both the University of Basel and ETH Zurich as well as partner institutions such as the University Children’s Hospital of Basel and the Swiss Tropical and Public Health Institute in Basel. Experts in systems biology, medicine and various areas of life sciences, engineering, social sciences and information technology will collaborate in a transdisciplinary approach to improve health care for children. The focus will be on countries with limited resources, but with the potential to implement solutions worldwide.

Unique research focus

BRCCH is unique in that rather than supporting individual research projects, it supports research streams. Each research stream is a novel form of interdisciplinary collaboration essential for addressing the complexity of a process which covers defining a health problem developing the clinical solution, and testing the clinical treatment for large-scale application.

The BRCCH will focus on four main areas of pediatric research: diabetes, infectious diseases/immunology, cardiorespiratory diseases, and the restoration of bodily functions through regenerative surgery. A number of research areas have already been defined within these key fields; the research approaches will be geared to digital and mobile healthcare solutions and to cell-based therapies.

Professor Sai Reddy’s research focusing on engineering antibodies against infections with a view to setting up an antibody engineering and production pipeline including vaccination-testing machinery fits perfectly into the planned activities of the Botnar Research Centre for Child Health.

The Research Centre will begin its operational activities in Basel in early 2019 and will be expanded gradually.
SAI REDDY IN PERSON

Professor Sai Reddy has spent his academic career travelling between the US and Europe, particularly Switzerland.

Professor Reddy was born in 1980 in Hyderabad, India. When he was one, his family moved to the United States and he grew up outside Chicago. He attended the Northwestern University in Evanston, IL, USA, where he received B.S. (2003) and M.S. (2004) degrees in Biomedical Engineering. Sai Reddy completed his Ph.D. thesis at the École Polytechnique Fédérale de Lausanne (EPFL) in Bioengineering and Biotechnology in 2008, under the supervision of Prof. Melody Swartz and Prof. Jeffrey Hubbell. His research centered on developing a novel nanoparticle vaccine technology, and it earned him KPMG tomorrow’s market award in 2007. Prof. Reddy moved to University of Texas, Austin (USA) for his post-doctoral fellowship (2008), where he worked under the supervision of Prof. George Georgiou on protein and antibody engineering. The technology he co-developed on monoclonal antibody discovery without screening combined high-throughput DNA sequencing, bioinformatics, and synthetic biology and importantly, demonstrated how systems and synthetic immunology can impact biotechnology. After working as an Assistant Professor at the University of Colorado at Boulder for five months, he joined ETH in February 2012 as a tenure track Assistant Professor of Biomolecular Engineering. In July 2018 he was appointed Associate Professor for Systems and Synthetic Immunology.

– When did your enthusiasm for science and especially immunology begin?
I always excelled at math, so I naturally started thinking about a career in engineering sciences. But I was also fascinated by biology and considered pursuing a career in medicine too. I was lucky that by the time I began university, the field of biological engineering was becoming established; it seemed like a perfect fit for me.

– What is your main motivation for your work?
One of my main motivations is to educate and support the careers of young scientists so that they achieve their goals and make a long-lasting impact. I also want to bridge the gap between academic research and industry applications, so that there can be direct impact for new medicines and therapies.

– Which of your main findings are you especially proud of?
I’m still most proud of two main findings: one was during my PhD where I established a method for targeted vaccine delivery to lymph nodes using synthetic particles, which act essentially like plastic viruses and initiate strong protective immune responses while being very safe. This approach has been adopted by many researchers in both academic and industry. The other main finding is based on work I started as a postdoc but continue to this day in my group; it concerns the rapid discovery and engineering of antibodies. Antibody therapeutics are the dominant type of biological drugs because of their ability to target a wide variety of diseases (such as cancer, autoimmune disease, infectious disease). However, antibody drug discovery and development requires highly sophisticated methods, time, and resources — so it’s only feasible for a small segment of highly financed biopharmaceutical companies. We’re establishing methods based on DNA sequencing and machine learning, coupled to cellular engineering that accelerates the discovery and engineering of antibodies. The ultimate goal is to commoditise the market for antibody drugs, and make them accessible for a much wider range of diseases and indications.

– You’ve been at ETH Zurich and in Switzerland for the last six years; do you feel at home here?
Switzerland does indeed feel like home to me now. I love the simplicity and efficiency of living here — everything functions and works in such a professional and effective way. This spans the transportation system, healthcare, and the political system (which, as a US citizen, is something I’m acutely aware of these days). Naturally, many of the positive things about Switzerland are mirrored by ETH. It’s an amazing place to work and do research; the infrastructure and resources are world-class. The people it attracts, including students, faculty, and administrative support are all at the highest level. I consider myself extremely lucky to have found such a great place to pursue my career.
MISROCK FOUNDATION AND PROFESSOR SAI REDDY – A SUCCESS STORY

Almost nine years ago, the Misrock Foundation decided to support the newly created professorship Biomolecular Engineering. The appointment of Sai Reddy as assistant professor in November 2011 was the beginning of a success story that was extremely positive for both sides.

“I’m delighted that Professor Sai Reddy, whose professorship is funded by the Misrock Foundation, is so successful. Our donation is bearing fruit: Sai Reddy and his research team are an asset not only for the ETH Department of Biosystems in Basel, but also for us.”
Jean-Marc Joerin, President of Misrock-Foundation

“The generous donation from the Misrock Foundation allowed me to establish a new laboratory in Basel and to focus entirely on research and education. I’m most grateful to the Misrock Foundation for this opportunity.”
Sai Reddy

MILESTONES

2010
Initial funding of CHF 0.5 m from the Misrock Foundation with the announcement of the Biomolecular Engineering professorship.

30.11. 2011
Appointment of Sai Reddy as tenure-track Assistant Professor by the ETH Board.

8. 3. 2012
Sai Reddy takes up post as Assistant Professor. Funding of CHF 2 m from the Misrock Foundation.

20.11. 2012
Introductory lecture by Professor Sai Reddy.

2013
Funding of CHF 1 m from the Misrock Foundation.

2014
Funding of CHF 1 m from the Misrock Foundation.

2015
Funding of CHF 1 m from the Misrock Foundation.

1. 2. 2016
Reappointment as Assistant Professor for a further 3 years. Funding of CHF 1 m from the Misrock Foundation.

2017
Funding of CHF 1 m from the Misrock Foundation.

JULY 2018
Appointment as Associate Professor at ETH Zurich. A further CHF 168,000 in funding for Professor Sai Reddy and the BSSE.
New platform called “plug-and-(dis)play hybridomas for reprogramming the antibody specificity of immune cells”.

By applying CRISPR-Cas9 to the antibody producing hybridoma cells, this technology opens up a number of future opportunities, such as the inexpensive and very fast production of antibody production. Professor Reddy filed a European patent application for this technology in 2016.

Targeted vaccine delivery to lymph nodes using synthetic nanoparticles

This new method initiates strong protective immune responses while being very safe. This approach has been adopted by many researchers in both academic and industry. The method was granted a US patent in 2012.

In 2014 Professor Sai Reddy became project leader of the “NCCR Molecular Systems Engineering” and in 2015 a member of the “Infection and Immunity Zurich” network.

Professor Reddy also established the “Biomolecular Engineering and Immunotechnology” master class. In November 2013, he also received the “Golden Owl award”. This prize honours lecturers who have provided exceptional teaching. The Owl is awarded once a year by the students association of ETH Zurich (VSETH) to one lecturer per department.

Group 2018:
2 Senior Scientists,
3 post-doctorates,
15 doctoral candidates,
5 Master students

2012 – 2018:
7 post-doctorates,
18 doctoral candidates,
16 Master’s theses

4 patents
2 granted,
2 pending

Collaboration with
Roche, Novartis,
NBE Therapeutics,
UCB-Celtech,
Specifica, aiNET

SOME STATISTICS

Professor Sai Reddy has achieved important research results which have led to a whole bunch of publications and patents. An excerpt of some of his work is given here:

**Systems Analysis Reveals High Genetic and Antigen-Driven Predetermination of Antibody Repertoires throughout B Cell Development**

In a recent study, Sai Reddy and his team implemented an integrated experimental-computational systems immunology framework to quantify the balance of nature versus nurture in antibody repertoires across B cell development in mice. They found a dynamic balance of genetic and antigen-driven predetermination and stochastic variation, which was true across B-cell development, various antigens, and repertoire components. The study was published in Cell Reports 2017 (Greiff et al., Cell Reports, 2017).

**Reprogramming MHC specificity by CRISPR-Cas9-assisted cassette exchange**

In another recently completed study Sai Reddy and his team have reprogrammed the MHC-specificity of a mouse macrophage cell line by immunogenomic engineering. The goal was to demonstrate a proof-of-concept for MHC-allelic replacement that could be used in the future for improving donor-host matching, often a major challenge in allogeneic stem cell transplantations in cancer. This study has been published in Scientific Reports 2017 (Kelton et al., Scientific Rep, 2017).

**Master’s Theses at the Laboratory for Systems and Synthetic Immunology**

Of the 16 students that completed Master’s theses at the Lab, a whole bunch continued their career within the field of Molecular Biology/Immunology Research. Three went on to do their doctorate at the Lab and two at the University of Oxford, UK, and Delft University of Technology in Delft, Netherlands respectively.

Another three found a job at Roche Pharmaceuticals and one at NBE Therapeutics Ltd., both in Basel, Switzerland.

A further former Master’s student is now a graduate research assistant at the German Research Foundation in Frankfurt, while one is at the European Molecular Biology Laboratory in Heidelberg, both in Germany.
HATCHERY FOR PROMISING YOUNG CAREERS

During the last six years Professor Reddy’s group has been growing steadily, as have the alumni. Several former group members have started a promising career in the field of immunology research. Some of them are portrayed below, and describe the impact Professor Reddy had on their career.

Currently Associate Professor at the Department of Immunology, University of Oslo in Norway

Professor Victor Greiff leads the Computational and Systems Immunology research group, which aims to detect patterns within the immune system using artificial intelligence. The goal is to generate diagnostic predictions for disease progression and state. In addition, Professor Greiff and his group are computationally modelling the binding of antibodies and T cells to antigens in order to develop enhanced vaccines and immunotherapeutics.

“My time as a PostDoc in Professor Reddy’s group was extremely important for me. Professor Reddy gave me full freedom and support to follow my scientific curiosity. Also, I could count on his full support at any time during the application process for the professorship. Despite the geographical distance (Norway-Switzerland) we are still in active contact and regularly exchange the latest research results in systemic and synthetic immunology.”

Currently Senior Scientist at NBE-Therapeutics, Basel, Switzerland

Dr. Ina Hellmann leads a team in the preclinical development of next-generation antibody-drug conjugates (ADCs) as improved treatment options for cancer patients. ADCs are comprised of an engineered tumor-specific antibody coupled to a highly potent cellular toxin, thereby combining antigen specificity and highly potent cytotoxicity in a single molecule. The targeted delivery of the cytotoxin via the antibody portion results in increased anti-tumor efficacy and increased safety due to lower toxicity on normal tissues. The group works on the entire preclinical ADC development process from antibody discovery via expression and characterisation of antibodies, enzymatic conjugation to cellular toxins using NBE-Therapeutics’ proprietary SMAC technology® to in vitro and in vivo evaluation of ADCs. The group has successfully identified promising lead ADC product candidates for several oncology targets.

“What makes Professor Reddy stand out is his focus on developing innovative methods with a clear vision for use in clinical applications. With Prof. Reddy’s support and guidance, I was working in a very close, successful collaboration with NBE-Therapeutics, which allowed me to directly translate my research findings into the development of therapeutic drugs.”
Dr. Tarik Khan leads a team in the late-stage formulation and process development group at Roche, where they focus on characterizing and optimizing how therapeutic proteins (e.g. monoclonal antibodies) interact and behave not only with themselves but also with excipients, packaging material, administration equipment and during processing. Thus the final goal is to ensure that the drugs remain safe and efficacious after manufacturing, shipping, storage, and administration to the patient. The group is working both on the development of pipeline projects – designing and executing studies to be ready for human clinical trials, commercial technology transfer, and filing for market approval – and also doing research to better understand observed issues.

“Prof. Reddy’s passion for science inspired me to strive for scientific excellence. To this day, I value Prof. Reddy’s advice and discussions, both scientifically and regarding career development.”

aiNet leverages artificial intelligence and large scale networks to help pharmaceutical and biotechnology companies discover biologics – medicines from biological sources, mainly antibodies, which are used for the treatment of cancer, infections and immunodeficiency disorders.

“Professor Sai Reddy has been a sound guide and an inspiration, supporting my professional ventures while holding it all together. His generosity is exceptional, and I hope to carry his kind nature with me.”
ADDITIONAL FUNDING

Besides the generous funding provided by the Foundation of S. Leslie Misrock, Professor Sai Reddy and his group have received additional funding of over CHF 6 million since 2012 from the following organisations:


ETH Domain strategic focus area of Personalized Health and Related Technologies (PHRT)

In 2017, Sai Reddy together with Prof. Alfred Zippelius (Senior Physician in Oncology and Head of the Laboratory for Cancer Immunology) from the University of Basel received a grant from the Personalized Health and Related Technologies (PHRT) for the project “Genetically engineered humzane mice for personalized drug discovery in cancer immunotherapy”.

European Research Council (ERC) Grant 2015

As one of seven researchers at ETH Zurich, Sai Reddy received the ERC Grant in 2015 to work on the profiling of the molecular network of antibody responses by using the methods of high-throughput DNA sequencing and computational biology.

Grand Challenges Explorations (GCE) fund by the Bill & Melinda Gates Foundation for the project “Measurement of Somatic Hypermutation Induced by C3d Antibody-Dependent Cells”.

ETH Research Grant


Swiss National Science Foundation

“Quantitative molecular analysis of polyclonal memory B cell responses” (funding period: 06. 2013 – 06. 2016)

Swiss Commission for Science and Technology and Innovation (CTI)

“Development of functional therapeutic antibodies via next-generation DNA sequencing and bioinformatics analysis of whole B cell antibody repertoires” in collaboration with the early stage biotechnology company NBE-Therapeutics in Basel, Switzerland (funding period: 07. 2013 – 07. 2016)

SystemsX.ch

The Swiss Initiative in Systems Biology

PUBLICATIONS

2018


2017


2016


Kalton W, Peach T, Mullie S, Reddy ST, Surveying the delivery methods of CRISPR/Cas9 for ex vivo mammalian cell engineering, China (2016).


2015


2014


PATENTS


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2018

ETH Zurich Foundation
Weinbergstrasse 29
CH-8006 Zurich
+41 (0)44 633 69 66
info@ethz-foundation.ch
www.ethz-foundation.ch