

Can new drugs be tested with computers? EU-funded team explores the future of tuberculosis drugs testing

Catania, 14 December 2018

Today the STriTuVaD consortium published the technical report "[A modelling framework to simulate the dynamics of the human immune system](#)". Led by [Etna Biotech](#), an innovative R&D company based in the south of Italy, the STriTuVaD consortium coordinates some of the research excellences in Europe. The overall goal of the project is to demonstrate how advanced computer modelling and simulation can be used to reduce the costs of the clinical trials required to test the efficacy of new therapies for tuberculosis.

Tuberculosis (TB) is one of the world's deadliest infectious diseases ([Global WHO TB report 2016](#)): one third of the world's population, mostly in developing countries, is infected with TB ([O'Garra A., et al., 2013](#)). But TB is increasingly becoming problematic for developed countries, due to the increased mobility of the world population and the appearance of several new bacterial strains that are multi-drug resistant (MDR). There is now a growing awareness that TB can only be effectively fought by working globally, starting with countries like India, where the infection is endemic. Once a person presents with the active disease, the most critical issue is the current duration of therapy including high costs of treatment, the increased chances of non-compliance (which increases the probability of developing an MDR strain), and the time the patient is still infectious.

One promising possibility to shorten the duration of the therapy is new host-reaction therapies (HRT) offered in combination with the antibiotic therapy.

The endpoints in the clinical trials for HRTs are time to inactivation and incidence of recurrence. With inactivation, it is possible, in some cases, to have a statistically powered evidence for efficacy in a Phase II clinical trial; however, recurrence almost always requires a Phase III clinical trial with thousands of patients involved and huge associated costs.

The STriTuVaD project will extend the Universal Immune System Simulator, developed by Prof Francesco Pappalardo at the University of Catania, to include all relevant determinants of such a clinical trial. The project will establish predictive accuracy against the individual patients recruited in the trial, use it to generate virtual patients and predict their response to the HRT being tested, and then combine them with the observations made on physical patients using a new in silico-augmented clinical trial approach that uses a Bayesian adaptive design. This approach, where found effective, could drastically reduce the cost of innovation in this critical sector of public healthcare and make advanced therapies available at reasonable costs.

About STRITUVAD:

Acronym: STriTuVaD

Title: In Silico Trial for Tuberculosis Vaccine Development

Project ID: 777123

Funded by the European Commission under: H2020-EU.3.1.5. - Methods and data

Duration: From 2018-02-01 to 2022-07-31

Total cost: EUR 5 050 656,25

Consortium:

- ETNA BIOTECH SRL, Italy
- UNIVERSITÀ DEGLI STUDI DI CATANIA, Italy
- THE UNIVERSITY OF SHEFFIELD, United Kingdom
- ARCHIVEL FARMA, SL, Spain
- STICHTING TUBERCULOSIS VACCINE INITIATIVE, Netherlands
- INFECTIOUS DISEASE RESEARCH INSTITUTE, United States
- THE ALL-INDIA INSTITUTE OF MEDICAL SCIENCES, India
- ALMA MATER STUDIORUM – UNIVERSITY OF BOLOGNA, Italy

About the partner institutions

The University of Sheffield

With almost 29,000 of the brightest students from over 140 countries, learning alongside over 1,200 of the best academics from across the globe, the University of Sheffield is one of the world's leading universities.

A member of the UK's prestigious Russell Group of leading research-led institutions, Sheffield offers world-class teaching and research excellence across a wide range of disciplines.

Unified by the power of discovery and understanding, staff and students at the university are committed to finding new ways to transform the world we live in.

Sheffield is the only university to feature in The Sunday Times 100 Best Not-For-Profit Organisations to Work For 2017 and was voted number one university in the UK for Student Satisfaction by Times Higher Education in 2014. In the last decade it has won four Queen's Anniversary Prizes in recognition of the outstanding contribution to the United Kingdom's intellectual, economic, cultural and social life.

Sheffield has six Nobel Prize winners among former staff and students and its alumni go on to hold positions of great responsibility and influence all over the world, making significant contributions in their chosen fields.

Global research partners and clients include Boeing, Rolls-Royce, Unilever, AstraZeneca, Glaxo-SmithKline, Siemens and Airbus, as well as many UK and overseas government agencies and charitable foundations.

To read other news releases about the University of Sheffield, visit <http://www.shef.ac.uk/news>

The Insigneo Institute for *in silico* Medicine

The Insigneo Institute for *in silico* Medicine is a collaborative initiative between the University of Sheffield and Sheffield Teaching Hospitals NHS Foundation Trust. It is a multidisciplinary collaboration between over 150 academics and clinicians to develop computer simulations of the human body and its disease processes that can be used directly in clinical practice to improve diagnosis and treatment.

In silico medicine (also known as "computational medicine") is the application of *in silico* research to problems involving health and medicine. It is the direct use of computer simulation in the diagnosis, treatment, or prevention of a disease. More specifically, *in silico* medicine is characterised by modelling, simulation, and visualisation of biological and medical processes in computers with the goal of simulating real biological processes in a virtual environment. This is almost certainly the most sophisticated application of computing technology in healthcare, and Sheffield has become the UK's principal centre for this work. Insigneo performs cutting-edge research in areas of fundamental and applied biomedical

modelling, imaging and informatics, as it pursues the research agenda of the Virtual Physiological Human initiative.

The Institute's work will bring about a transformational change in healthcare through multidisciplinary collaborations across many strategic areas, which will include personalised diagnosis and treatment and improvements in independent, active and healthy ageing. For more information please visit: www.insigneo.org or contact news@insigneo.org.

The University of Catania

The University of Catania was founded in 1434. Today it is one of the Italy's largest universities with 17 Departments and 2 Didactic Units, about 50000 students and about 1400 professors and researchers (www.unict.it/en).

The Department of Drug Sciences main activities are higher education and research in drug design, biochemistry and related topics (<http://www.unict.it/en/drug-sciences>).

Inside the Department, the Computational Systems Biomedicine Research Group (COMBINE) drives the research in applying computational methodologies to the field of biomedicine.

The goal of the group is to develop computational/mathematical models for better understanding of biomedical processes and design of new experiments. The expertise ranges from computational models based on cellular automata and agents to equation based models.

The modeling framework developed by the COMBINE group has been extensively used to model the immune response elicited by vaccines and immunotherapies against various diseases, including cancers.

TuBerculosis Vaccine Initiative

The TuBerculosis Vaccine Initiative (TBVI) is a non-profit foundation that facilitates the discovery and development of new, safe and effective TB vaccines that are accessible and affordable for all people. TBVI integrates, translates and prioritises R&D efforts to discover and develop new TB vaccines and biomarkers for global use. TBVI provides essential services that support the R&D efforts of its consortium partners – 50 partners from academia, research institutes and private industry in the TB vaccine field. These services include project identification, design and development; project management; resource mobilisation; knowledge development, exchange and networking; and technical advice and support for product and clinical development. www.tbvi.eu

Alma Mater Studiorum - University of Bologna

The University of Bologna, founded in 1088, is the oldest university in continuous operation, as well as one of the leading academic institutions in Italy and Europe. It is one of the most prestigious Italian universities, commonly ranking in the first places of national rankings. It was the first place of study to use the term *universitas* for the corporations of students and masters, which came to define the institution located in Bologna, Italy. The University's crest carries the motto *Alma mater studiorum* and the date A.D. 1088, and it has about 86,500 students in its 11 schools. It has campuses in Ravenna, Forlì, Cesena and Rimini and a branch center abroad in Buenos Aires, Argentina. It also has a school of excellence named Collegio Superiore di Bologna. In the STriTuVaD project it participates with the **Department of Industrial Engineering**, which is active in research, and provides education in different fields of Engineering: Aerospace, **Biomechanics**, Power, Management, Mechanical, Nuclear, Technical Physics, and Metallurgy. The Biomechanics Group is led by Prof Luca Cristofolini and Prof Marco Viceconti, who is a world-class specialist in *in silico* trials.

Archivel Farma

Archivel Farma is a biotechnology R&D company that develops immunotherapeutic agents to respond to uncovered medical needs. It is currently developing the RUTI® vaccine for the treatment of tuberculosis which is in a phase II clinical trial. www.archivelfarma.com

All India Institute of Medical Sciences, New Delhi

Creating a country imbued with a scientific culture was Jawaharlal Nehru's dream, and immediately after independence he prepared a grand design to achieve it. Among the temples of modern India which he designed, was a centre of excellence in the medical sciences. Nehru's dream was that such a centre would set the pace for medical education and research in Southeast Asia, and in this he had the wholehearted support of his Health Minister, Rajkumari Amrit Kaur.

The health survey and development committee, chaired by Sir Joseph Bore, an Indian Civil Servant, had in 1946 already recommended the establishment of a national medical centre which would concentrate on meeting the need for highly qualified manpower to look after the nation's expanding health care activities. The dreams of Nehru and Amrit Kaur and the recommendations of the Bore Committee converged to create a proposal which found favor with the government of New Zealand. A generous grant from New Zealand under the Colombo Plan made it possible to lay the foundation stone of All India Institute of Medical Sciences (AIIMS) in 1952. The AIIMS was finally created in 1956, as an autonomous institution through an Act of Parliament, to serve as a nucleus for nurturing excellence in all aspect of health care.

All-India Institute of Medical Sciences was established as an institution of national importance by an Act of Parliament with the objects to develop patterns of teaching in Undergraduate and Post-graduate Medical Education in all its branches so as to demonstrate a high standard of Medical Education in India; to bring together in one place educational facilities of the

highest order for the training of personnel in all important branches of health activity; and to attain self-sufficiency in Post-graduate Medical Education.

The Institute has comprehensive facilities for teaching, research and patient-care. As provided in the Act, AIIMS conducts teaching programs in medical and para-medical courses both at undergraduate and postgraduate levels and awards its own degrees. Teaching and research are conducted in 42 disciplines. In the field of medical research AIIMS is the lead, having more than 600 research publications by its faculty and researchers in a year. AIIMS also runs a College of Nursing and trains students for B.Sc.(Hons.) Nursing post-certificate) degrees.

Twenty-five clinical departments including four super specialty centers manage practically all types of disease conditions with support from pre- and Para-clinical departments. However, burn cases, dog-bite cases and patients suffering from infectious diseases are not entertained in the AIIMS Hospital. AIIMS also manages a 60-bedded hospital in the Comprehensive Rural Health Centre at Ballabgarh in Haryana and provides health cover to about 2.5 lakh population through the Centre for Community Medicine.