

PROFESSOR ROLAND MARTIN AND DR THOMAS SPIRIG ON THE UNIVERSITY OF ZURICH'S LAUNCH OF A CLINICAL AND TRANSLATIONAL RESEARCH PROGRAMME IN MULTIPLE SCLEROSIS AND OTHER AREAS

Advancing biomedicine

Academic hospitals in many countries, including the University Hospital Zurich, Switzerland, find themselves in the difficult situation of having to deliver state-of-the-art healthcare, develop new therapies at the forefront of medicine, provide excellent medical education and pursue world class research. Furthermore, affiliated universities and their basic scientists need to be able to engage with the exchange process whereby basic science advances are translated into the clinic and back again.

Physician-scientists are at the centre of this dilemma. A lack of time for research, the ever-growing complexity of reimbursement for healthcare and difficulties in implementing research infrastructures in an often care-focused environment are some of the challenges that need to be addressed. Moreover, access to well-defined patient groups or biosamples/health data and collaborative networks between clinicians and basic scientists need to be established in order to advance biomedicine and bring scientific progress to the patient.

Kick-start

The University of Zurich has taken an innovative step to kick-start clinical and translational research with a set of clinical centre grants. Launched in 2012, the Clinical Research Priority Program (CRPP) was initiated as a funding instrument to specifically promote strategic areas of clinical research at the university.

The University of Zurich funds 11 CRPPs in the following areas:

- Multiple sclerosis;
- Human haematolymphatic diseases;
- Molecular Imaging Network Zurich;
- Neurorehabilitation;
- Unresectable liver tumours;
- Novel tissue-engineered skin grafts;
- Rare Disease Initiative Zurich;
- Sleep and health;
- Small RNAs in the pathogenesis, diagnosis and therapy of human diseases;
- Tumour oxygenation; and
- Viral infectious diseases.

See: www.uzh.ch/research/priorityprograms/clinic_en.html

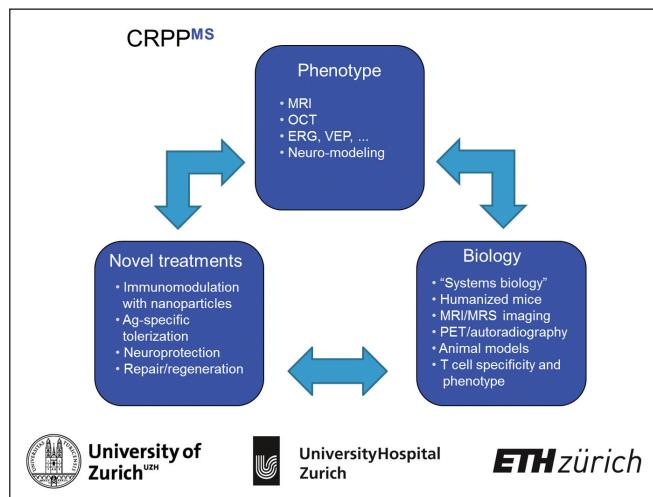


Fig. 1 Schematic depiction of how research in the CRPP^{MS} spans from the definition of disease phenotypes over biological studies to developing novel treatment

The CRPP builds on the university's excellent reputation in research and teaching. In particular, it attaches great value to knowledge exchange between basic research, applied research and clinical care. A main goal of the new programme is to form sustainable scientific networks between basic scientists at the University of Zurich and clinicians at the five affiliated university hospitals. In addition, the CRPP is committed to promoting young scientists in the field of clinical research by supporting doctoral and postdoctoral researchers and creating assistant professorships.

Following the announcement to initiate the new funding programme for clinical research in early 2012, the University of Zurich selected 11 individual CRPPs in a competitive process for long term funding. All 11 programmes established by the end of 2012 are multidisciplinary, highly collaborative and share a translational approach.

Individual CRPPs either focus on a common theme (e.g. tumour oxygenation) or address a set of related diseases (e.g. viral infectious diseases or human haematolymphatic diseases). The CRPPs 'Molecular Imaging

Network Zurich' and 'Small RNAs' investigate methodological approaches across various disciplines. Alternatively, the research programmes may focus on a more specific disease, such as multiple sclerosis (MS).

MS

The CRPP^{MS} investigates disease heterogeneity in MS, a prototypic autoimmune disease which affects the central nervous system and leads to neurological deficits in young adults. Like all human diseases with a complex genetic background, MS is characterised by disease heterogeneity at all levels, from the molecular etiology – including a large set of risk-conferring genes and several environmental factors – through its immunological mechanisms and pathological findings, to its imaging and clinical presentation, including differential response of patients to treatment.

While MS patients are clinically followed in neurology departments, pursuing research on the diverse aspects that are involved in disease heterogeneity requires a highly interdisciplinary collaboration between neurologists, ophthalmologists, neuroradiologists, biologists, immunologists, imaging experts, engineers, and scientists with expertise in modelling, bioinformatics and proteomics.

Themes

The CRPP^{MS} brings together scientists from these different fields and the University of Zurich, the University Hospital Zurich and the Swiss Federal Institute of Technology in subprojects, which are partitioned into three major themes (Fig. 1).

The first set of questions aims at defining pathogenetically meaningful phenotypes of MS by magnetic resonance imaging (MRI), optical coherence tomography (OCT), electrophysiological measures and neuromodelling.

In the second theme, the biological basis of these phenotypes is examined by developing humanised mouse models, by disease-focused systems biology approaches, by high resolution MRI and autoradiography with positron emission tomography ligands on MS brain tissue, and by linking specific subforms of MS with the antigen-specificity and function of brain-infiltrating T cells in MS.



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The third theme develops novel treatments that address major unmet medical needs in MS. Well-defined patient groups from the phenotyping studies and outcomes derived from research under the other themes are very important for designing proof-of-concept clinical trials (phase IIa) in which novel treatments are assessed with respect to early indication of efficacy and mechanism of action.

Challenge

Establishing the translational research infrastructure – i.e. a clinical trials team of nurses and physicians and a regulatory expert, a biobank and research database, as well as a seminar series, teaching interactions and training of young investigators, nurses, and physicians – represents an important challenge.

The CRPP funding instrument has provided the necessary support to start this endeavour and further facilitates investment from additional sources, e.g. industry and third party funding. The experience from the first funding period indicates that the CRPP effectively promotes the formation of highly interdisciplinary networks for translational research.

An ongoing review of the current CRPPs will locate the most successful programmes, which will be supported for an additional funding period.

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