



Keynote Lecture XIII

Translational Research in Switzerland: From Human Vascular Cells to Clinical Trials

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Born 1953 in Zürich, Switzerland, Thomas F Lüscher studied medicine at the University of Zürich and obtained his MD in 1978 at the same institution. From 1979 to 1984 he was a fellow in internal medicine and cardiology at the University Hospital Zürich and then worked in the US at the Mayo Clinic in cardiovascular research and cardiology for almost three years. Upon his return to Switzerland in 1987 he took a position as associate consultant in cardiology at the Department of Research at the University Hospital Basel. He was named Professor of Medicine in 1992 and held a position as consultant in cardiology and Professor of Medicine at the University of Bern, Switzerland. In 1996 he was appointed Head of Cardiology at the University Hospital Zürich, Switzerland and Professor of Cardiology at the same University. Thomas F Lüscher's research group has a special interest in vascular disease, endothelial factors and atherosclerosis.

Medicine as a science and an art aims to use the knowledge gained to the benefit of a patient. Scientific discovery, therefore, in this type of research always is directed towards its potential practical use to diagnose or treat a disease. In Western countries and in particular in Switzerland cardiovascular disease is by far the most important cause of morbidity and mortality. Myocardial infarction, sudden death as well as stroke account for about 45% of mortality. Moreover, cardiovascular diseases are an important cause for doctors' visits as well as hospitalizations. Therefore, also pharmaceutical industries that are engaged in research and development assign a large part of their resources to the discovery of new tools for cardiovascular disease.

Research is practiced at different levels, i.e. genes, cells, tissues, organisms as well as populations. In practice, cardiovascular research oscillates between these different levels and the knowledge gained at each of these levels leads to new questions and projects in other areas.

By far the most important problems in cardiovascular medicine occur due to vascular dysfunction leading to ischemia of vital organs such as the heart, brain and kidney. Therefore, the understanding of the cellular and molecular mechanisms of vascular diseases is in the center of the research interest. Since atherosclerosis is mainly a disease of the intima, endothelial cells as well as the other components involved in atherosclerosis such as monocytes, platelets and alike have attracted most attention. Animal models with specific transgenes or knockouts of genes of interest, e.g. apolipoprotein-E, p66 as well as JNK, have allowed to better understand vascular dysfunction with ageing, the presence of hypercholesterolemia or other conditions. Identified targets have to be confirmed in small proof of concept studies involving patients with specific diseases. In cardiovascular medicine this is done mainly in the forearm circulation, an easy accessible surrogate circulation to test hypothesis and new drugs. Concepts confirmed in such a surrogate circulation can then be tested more extensively in the coronary circulation or with hemodynamic assessment in the cardiac catheterization laboratory. Large clinical trials assessing combined endpoint of morbidity and mortality or mortality alone are, however, a necessity to finally translate a new concept into clinical practice. These different levels of research do require an interdisciplinary team involving biologists, research physicians, cardiologists as well as clinical epidemiologists.

Thus, translational research really is a more appropriate term for clinical research in general as it aims to bring basic concepts focusing on cellular and molecular mechanisms to the bedside.