Towards nanomedicine

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Throughout the existence of mankind, man has lived with the expectation to die quite young from violent external factors or from infectious diseases. During the 20th century, there has been considerable progress in world health, but this can mostly be attributed to improvements in living conditions – hygiene, access to safe drinking water, improved quality and variety of nutrition – rather than to breakthroughs in medical science or practice. As a result, life expectancy has increased dramatically, first in Europe and North America, but now also in countries such as China. Unfortunately, this is going hand in hand with an increase in the number of people affected by chronic or degenerative diseases, which also are at the origin of the current explosion of the costs of the healthcare system. Typically, treatment for these diseases is palliative in nature – mostly there is no cure and at best the progression of the disease can be delayed.

The basis for radical change in medical practice has to be found in molecular biology. During the last half century, the scientific understanding in this field has progressed very rapidly. It is now well accepted that most diseases have their origin in disturbances of the delicate balance in molecular processes taking place at the cellular and sub-cellular level. This is currently leading to a paradigm shift in medicine: from a focus on dysfunctional organs to an understanding of disease pathways at the cellular and molecular level. This shift is underlying the vision that genetic predisposition testing, early diagnosis, and personalized treatment will transform clinical practices, and lead to improved patient outcomes. Aspects of this vision are referred to as evidence-based medicine, personalized medicine, molecular medicine, or nanomedicine. Relevant to this paper, intended for physicists and engineers with an interest in nanotechnology, is the understanding that this vision can only come about by matching the progress in molecular biology with advances in medical microdevices, nanotechnology and physical instrumentation, and by inventing new ways of dealing with complex data, a field referred to as bioinformatics.

Biomarkers are signatures of relevant disease pathways. They can be molecules found in body liquids of patients, such as blood, urine, or saliva. It is then possible to design molecular targets (DNA molecules or antibodies) that bind selectively to such biomarkers. This can be exploited to develop biosensors for *in-vitro* molecular diagnostics tests. As an example, I will discuss the biosensors currently in development at Philips Research labs, which are based on magnetic detection. Such biosensors can be used for early detection of disease, thus for patient screening. However, a positive detection using a biosensor does not tell the physician where the diseased cells are located inside the body.

Biomarkers can also be specific biomolecules expressed on the surface of diseased cells, or contained within such cells. These can be targeted by contrast agents, administered into the bloodstream. Nanotechnology is an enabler for designing and manufacturing such contrast agents. By providing contrast agents with an appropriate physical label (a radioactive or magnetic atom, a fluorescent dye molecule or a nanoparticle), their prevalence in the body can be imaged using techniques such as positron emission tomography, magnetic resonance imaging, or optical imaging. Molecular imaging is an *in-vivo* technology that can be used to localize disease where it occurs inside the body. In the talk, I will present some existing and novel imaging modalities and their characteristics.

Finally, biomarkers can also be used to design targeted molecular drugs. Molecular imaging can be used to stage the disease progression, and to monitor the effectiveness of such therapies in individual patients. In addition, the imaging modalities can be used to trigger the controlled release of drugs from nanomolecular constructs, such as targeted microbubbles.