RIGHT

Combining complementary expertises in a multidisciplinary approach

RIGHT combines the strengths of 5 synergistic competence domains to overcome key technological barriers such as undesired interferon response and insufficient delivery, stability and targeting of RNAi to the appropriate cells. Rational and selective approaches are taken to generate efficient RNAi reagents, which include both chemically synthesized siRNA (small inhibiting RNA) and vector based gene therapy approaches using shRNA (small hairpin RNA). Strategies are developed for efficient delivery to cells and tissues of diseased organisms. Cell biology and disease models are used to allow addressing their function and effectiveness for the treatment of representative diseases.

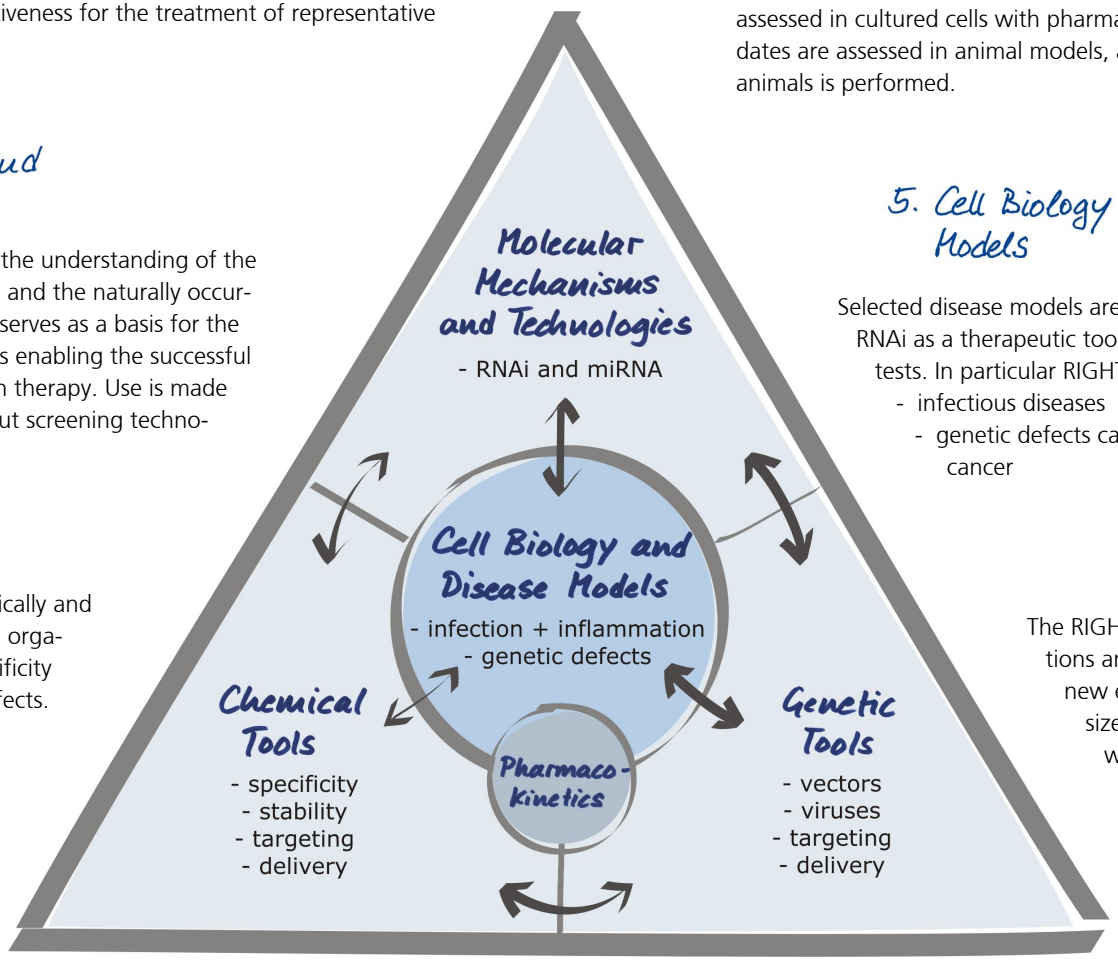
1. Molecular Mechanisms and Technologies

The RIGHT consortium aims at improving the understanding of the molecular processes associated with RNAi and the naturally occurring counterpart miRNA. This knowledge serves as a basis for the development of novel molecular strategies enabling the successful application of RNAi technology for human therapy. Use is made of large-scale libraries and high-throughput screening technologies.

2. Chemical Tools

Improved inhibitors are synthesized chemically and extensively tested in cell culture and living organisms in order to increase sensitivity, specificity and cost-effectiveness and reduce side effects. New tools include

- RNA mimics (e.g. with enhanced stability, sensitivity)
- RNA conjugates (e.g. with improved uptake properties)
- Delivery reagents



3. Genetic Tools

Potent viral or non-viral RNAi delivery vectors are generated and their features evaluated in relation to their chemical counterparts. Special emphasis is given to the development of tissue-specific and inducible systems.

4. Pharmacokinetics

For the development of a drug, synthetic or genetic RNAi reagents are first assessed in cultured cells with pharmacokinetic methods. Successful candidates are assessed in animal models, and extensive phenotyping of treated animals is performed.

5. Cell Biology and Disease Models

Selected disease models are used for the paradigmatic assessment of RNAi as a therapeutic tool. This will generate RNAi leads for clinical tests. In particular RIGHT is focussing on

- infectious diseases
- genetic defects causing degenerative diseases and cancer

The RIGHT partnership of leading research institutions and biotech SMEs will deliver tools such as new enabling technologies, chemically synthesized and genetically generated inhibitors with efficient delivery properties. Within 4 years the potential of RNAi to diagnose and successfully treat severe unvanquished diseases will be demonstrated and proof of principle provided for the value of RNAi as a therapeutic tool in living organisms.

RIGHT

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Exploiting the vast potential of RNAi for human therapy

The research initiative RIGHT "RNA Interference Technology as Human Therapeutic Tool" involves 22 research institutes and enterprises throughout Europe and is supported as an "Integrated Project" by the European Commission's Sixth Framework Programme for Research and Development (FP6) with a funding of 11 million Euros for the years 2005 to 2008.

Only recently it has been found that synthetically produced RNA sequences can be used to "silence" genes in human cells, a phenomenon that relies on the machinery of a naturally occurring gene silencing mechanism and that was lauded as 2002's 'breakthrough of the year' by Science magazine. The technology known as RNA interference (RNAi) gives relatively easy access to analyzing a gene's function and has had great impact on biological research since.

Building on the knowledge of gene sequences playing their role in diseases, RNAi molecules that specifically down-regulate the expression of dysfunctional genes can be created, thus enabling a targeted therapy.
The RIGHT project aims at exploiting and further developing the vast potential of RNAi to provide effective therapeutic tools for the treatment of severe diseases, based on an advanced understanding of the underlying mechanisms.
To achieve this ambitious goal, leading scientists of different disciplines have teamed up from Belgium, Denmark, Finland, Germany, Greece, France, Italy, Poland and Sweden.

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