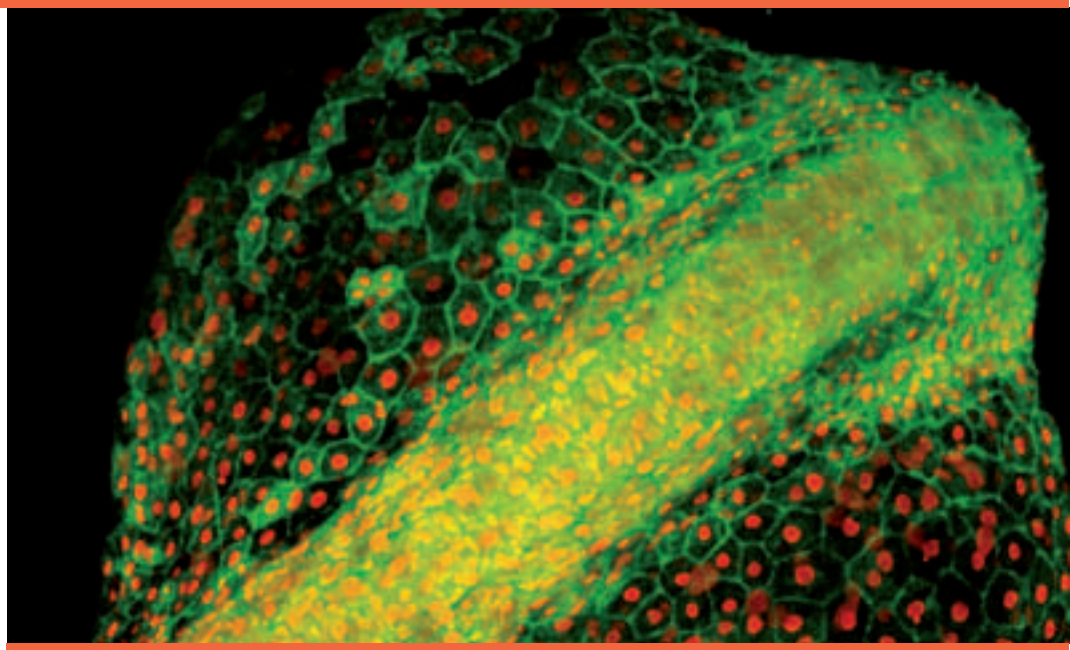
NEST
Pathfinder

TOWARDS PERSONALISED HEALTH

BIOEMERGENCES



Susceptibility to genetic diseases and responses to medical treatment are highly individual, depending in part on the genes and in part on the environment of the genes. BIOEMERGENCES is establishing strategies and tools to measure variations between unaffected healthy individuals, between those with the same genetic defect and between those receiving specific therapies. The result will facilitate the development of fully personalised treatments. It will also enable high throughput preclinical tests of anticancer drugs using an artificially assisted, high resolution microscope system.

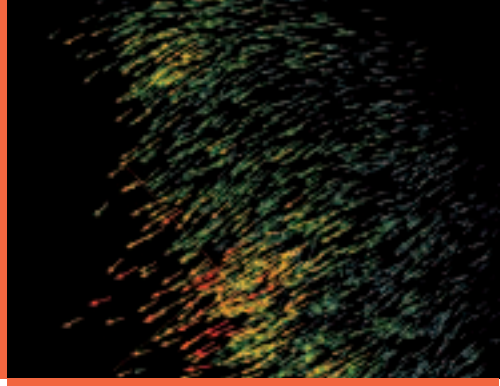
How to identify the similarities and differences between individuals is a fundamental question in biology. Advances in nanomedicine are driving developments in personalised medical therapy. However, the possibility of personalised medicine requires understanding the basis for individual variation; being able to record individual responses to defects as well as to treatments; and measuring the qualitative and quantitative differences between individuals or groups to identify the best approaches to therapy.

Susceptibility to disease and response to treatments are influenced both by individual genes and by their interaction with environments. No two living organisms react in exactly the same way to genetic defects or to medical treatments. The BIOEMERGENCES project, therefore, focuses on determining how to measure the individual differences in living beings at all levels.

Comparisons will be made on a vertebrate organism, the zebra fish (*Danio rerio*), using different fish populations (wild-type, mutant, treated and untreated). Zebra fish were chosen as they have a number of interesting characteristics, including transparent tissues, that allow high resolution *in vivo* imaging of cellular behaviour. These fish have already been validated as powerful models for investigations relating to humans, with growing interest from the pharmaceutical industry for their use in preclinical drug screening.

BIOEMERGENCES will record and reconstruct cellular behaviour at different scales.
The project's strategies will be applied to the characterisation of *in vivo* cell responses to a new class of anticancer drugs (Dbait) and to the establishment of individual susceptibility to holoprosencephaly, a condition which results in dramatic abnormalities of the brain and face in a genetically deficient fish population.
This work will serve as a test bed for a European platform to considerably enhance performance in the screening of new therapies and drug combinations.

" 'Artificial assistance' to help analyse susceptibility to genetic diseases and individual responses to treatments."



Individuality is controversial

Determining how much and in what way one individual differs from another is subject to considerable controversy as the answer depends on human perception, interpretation, culture and context. A scientific definition of the difference between two individuals from the same species is important, not least because of its social implications.

The BIOEMERGENCES project will attempt to measure and model individual differences using a non-mammalian vertebrate model that would allow high throughput *in vivo* investigations for future pharmaceutical screening. The complexity of this work involves a highly interdisciplinary and mainly academic team with world class expertise in developmental biology, toxicology, computational vision, applied mathematics, cognitive science, computer science and optical physics.

BIOEMERGENCES will use the latest developments in optical physics for four-dimensional (4D) microscopy imaging. The project's consortium has already developed a common language to express very different perspectives when dealing with biological objectives at the nano level, cellular level or at the level of the whole organism. The project will apply mathematical and computational tools to reconstruct and compare individual traits.

Advances expected from BIOEMERGENCES include the design of suitable markers to enable measurement of biological parameters as well as development of a standardised format to allow mathematical manipulation. Work will include validation of the selective plane illumination microscope (SPIM) prototype, built at the European Molecular Laboratory, for imaging the whole zebra fish embryo with resolution at cell level for extended periods.

Progress will also be made in the conception of a database able to handle the vast amount of data (particularly 4D measurements) to be stored and processed, in systems modelling for the multiscale analysis and integration of differences measured at all levels.

Automated measurement

A key goal of BIOEMERGENCES is the specification of a European platform to provide biologists with systematic and automated comparison of cell behaviour in chosen organisms. It will provide sophisticated 'artificial assistance' to help analyse susceptibility to genetic diseases and individual responses to treatments. The result will be fast access to phenotypic traits, which is almost impossible with currently available tools.

Individual treatment response will be investigated by testing reaction to recently developed Dbait molecules, designed to act as intelligent anticancer drugs targeting tumours which are resistant to conventional treatments. Results of this part of the study should make a significant contribution to the evaluation of the therapeutic potential of Dbait molecules and to improving their design.

BIOEMERGENCES will play an important role in the development of personalised medical therapies that require an integrated understanding of biological processes at all levels. The project will aid the development of high throughput preclinical screening for anticancer drug treatments, particularly bi- and tri-therapy combinations, on non-mammalian organisms.

AT A GLANCE

Official Title
'In What' and 'How Much' are Individuals Similar and Different? Towards the Measurement of the Individual Susceptibility to Diseases or Response to Treatments

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