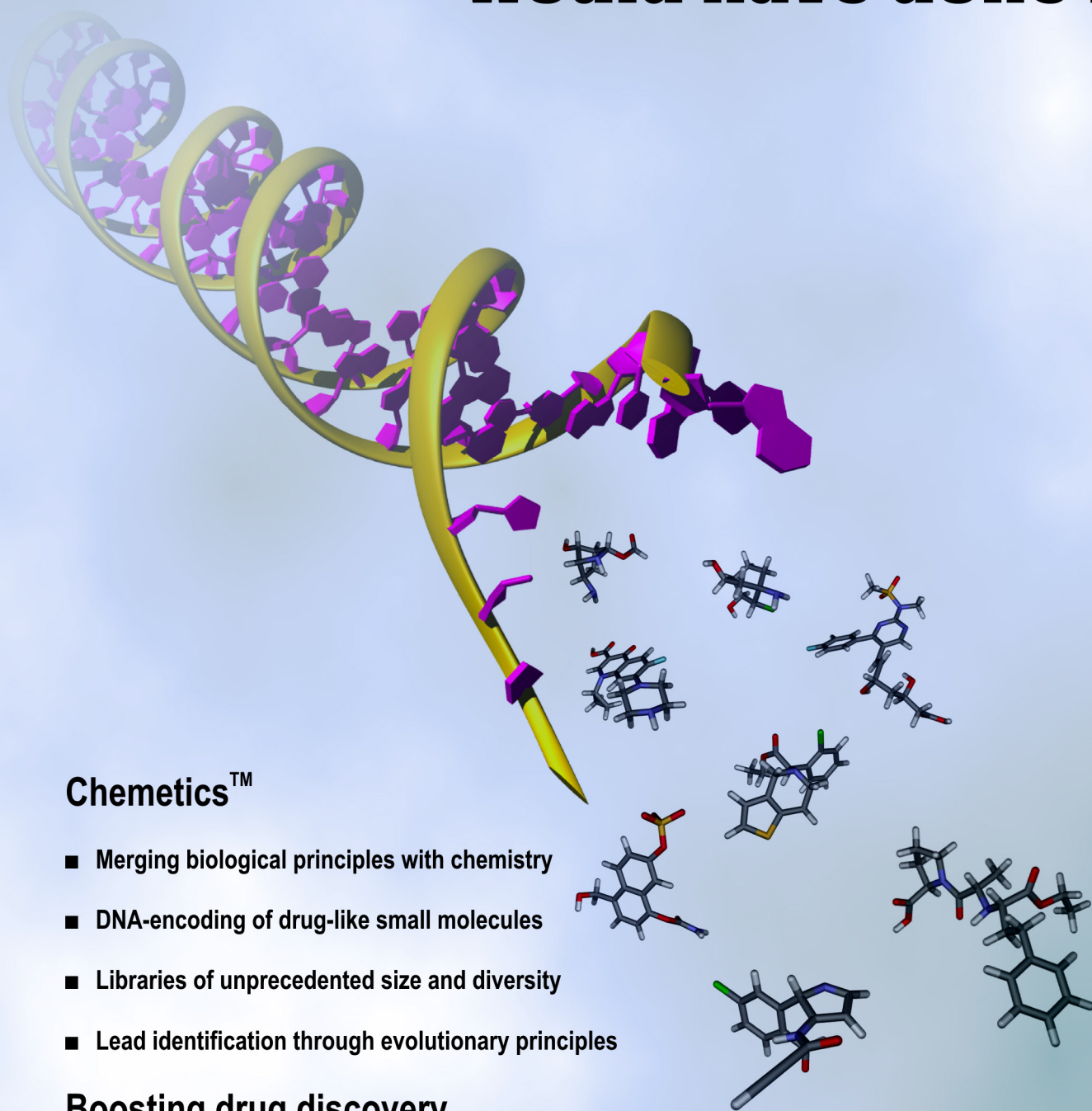


# Drug discovery as Nature would have done it



## Chemetics™

- Merging biological principles with chemistry
- DNA-encoding of drug-like small molecules
- Libraries of unprecedented size and diversity
- Lead identification through evolutionary principles

## Boosting drug discovery

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**Nuevolution**

# Harnessing the power of DNA

Rapid and efficient drug discovery is the Holy Grail of all pharma companies. Nuevolution is developing a wet chemistry approach that will allow rapid and accurate screening of billions of small drug-like molecules in months. This quantum leap in drug discovery is made possible through the development of a pseudo-genetic system in which DNA encodes small organic molecules. A number of advantages will result, including:

- Billions of drug-like molecules can be screened in months
- Assays are of very high accuracy
- Many leads per target
- High diversity of lead structures
- Broad IP protection of lead structures

Nuevolution's proprietary technology, Chemetics™, allows the DNA-templated synthesis of libraries of small organic molecules. The library is then screened by iterative cycles of selection and amplification, in a process very similar to the isolation of monoclonal antibodies from phage display libraries. Selection typically involves isolation of ligands by affinity-column chromatography where the target protein is immobilised on the column. Very small amounts of material are needed, and multiple rounds of selection and amplification are used to enrich the sample for the highest affinity and selectivity ligands.

## Chemetics is employed to make DNA molecules encode a large range of organic compounds

### A pseudo-genetic system

Nuevolution is dedicated to create an innovative technology combining the great potential of molecular evolution with combinatorial chemistry of small molecules. Chemetics mimics nature's genetic systems. In nature, genes (DNA molecules) encode peptides; at Nuevolution, Chemetics is employed to make DNA molecules encode a large range of organic compounds, including drug-like molecules. The process is very simple: it is a so-called one-pot process (meaning that the synthesis, screening and amplification of billions of molecules is performed in one test-tube), and is

*A new chemistry, now in development, promises to facilitate the screening of billions of small molecules in months.*

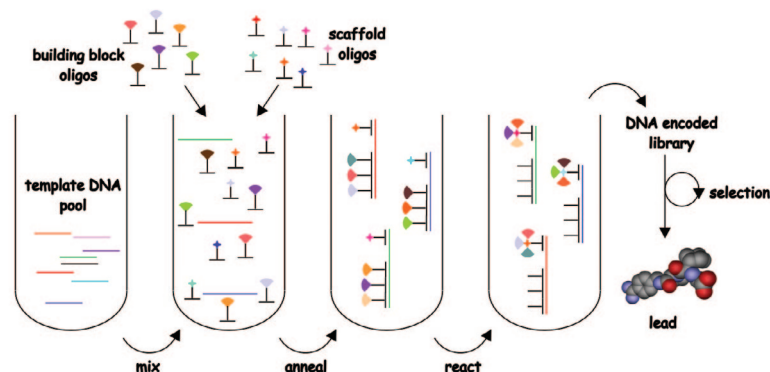


Figure 1. The Chemetics process

therefore extremely cost effective. It does not involve enzyme catalysis.

The Chemetics process is shown in Figure 1. In a first step, a library of, for example,  $10^9$  DNA templates are incubated with four sets of, for instance, 100 unique oligonucleotides, to each of which has been coupled a unique chemical moiety ('substituent'). The unique oligonucleotides anneal specifically to the templates. Then reactive groups of each complex react, to form a molecule whose composition is determined by the identity of the unique oligonucleotides, and hence the sequence of the individual templates. In other words, the sequence of the template determines which oligonucleotides anneal to it – and therefore also which chemical moieties that make up the final molecule.

The DNA template serves three functions: it directs the synthesis of the molecule, can be decoded to tell the synthetic history (and probable structure) of the molecule and it may be used to amplify the molecule, by amplification of the DNA template by PCR.

### Drug-like molecules of high structural diversity

The individual components of the Chemetics system are synthesised prior to the encoding process. Therefore, standard organic synthesis may be employed, and most molecular motives may be represented in the library. This includes most privileged structures of the medicinal industry. ■