drugs act on the worm neuromuscular system, as they do in humans. They demonstrate that they can stimulate the neurons responsible for egg-laying as well as some of the ones controlling body movements.

As these drugs still have an effect on worms carrying mutations in the insulin signalling pathway, identified previously as governing the worm aging processes, they also reveal a new role the nervous system in controlling worm longevity. The next step will be to test their anti-aging effects in higher organisms such as mice in order to find out if they could also help us live longer.

3 Evason, K. *et al.* (2004) Anticonvulsant medication extend worm life span. *Science* 307, 258–262
4 Wickelgren, K. (2004) As the worm ages: epilepsy drugs lengthen nematode life span. *Science*, 307, 193

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A tool for automated structure-based 3D-pharmacophore generation and its application to virtual screening

Virtual screening has established itself as a valuable *in silico* technique alongside the traditional HTS for new active compounds in the pharmaceutical industry. Pharmacophore modeling is the approach generally taken in presence of a set of known ligands, which are analysed for common functional groups responsible for specific drug–receptor interactions and their spatial alignment in 3D. The so-called pharmacophore comprizes chemical features such as hydrogen bonding, charge transfer, electrostatic and hydrophobic interactions. Alternatively, a resolved ligand–receptor complex can be analyzed in a structure-based approach typically linked to docking, where small molecules are fitted flexibly into the receptor and scored based on most favourable interactions. However, virtual screening of large databases via docking is expensive in CPU-time; thus, protein-based pharmacophore models provide an interesting, fast and powerful alternative.

Wolber and Langer now report LigandScout [1], which represents the first software tool with an automated method for pharmacophore model generation from structural protein-ligand data. Thereby, small organic molecules are extracted from high quality protein structures deposited in the Protein Data Bank (PDB) or any other databases containing protein-ligand complexes. The PDB is a repository optimized for protein structures with little regard of the correct description of small molecules, resulting in incomplete data. Thus, much attention is given to ligand perception and interpretation in terms of topology, hybridization states and bond types. In the final step, the pharmacophore is generated based on a set of rules for hydrogen bonding, charge and lipophilic interactions. This pharmacophore represents a model that is universal and comparable but still specific to reflect a certain mode of action as demonstrated and validated by application examples.

The resulting, automatically generated, pharmacophore model can be further analyzed, adapted and used for rapid database screening with any common screening platform. An example is Catalyst, a widely used pharmacophore modeling software package compatible with the above presented software tool making LigandScout a valuable contribution to virtual screening.

1 Wolber, G. and Langer, T. (2005) LigandScout: 3-D pharmacophores derived from protein-bound ligands and their use as virtual screening filters. *J. Chem. Inf. Comput. Sci.* 45, 160–169

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