

The future of drugs is all in the family

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In a first-ever comprehensive study of the species origins of nature-derived drugs, it is shown that drug-producing species are concentrated and clustered in a limited number of families, refuting the conventional view that as every nature species produces biologically active molecules, one can find drugs from almost any major block of species groups if one looks for them hard enough.

Whether you have a mild headache or you are running a fever, there is a high chance that the [drug](#) that is used to treat you comes from nature. Today, about half of the drugs on the market were discovered by screening collections of small molecules made by bacteria, fungi, snails, leeches and other such species.

In Singapore, the top selling drugs for treating common ailments that are derived from nature include No. 12 Aspirin (for pain, fever and inflammation), No. 2 Amoxil (antibiotic), No. 7 Procodin (for cough), No. 8 Beserol (muscle relaxant) and No. 3 Ventolin (for asthma and [chronic obstructive pulmonary disease](#)).

Worldwide, eight of the top 20 selling drugs available today are derived from nature, some of which include No. 2 [Lipitor](#) and No. 9 Crestor (both for treating cholesterol), No. 4 Advair Diskus (for asthma), No. 15 Lantus (for diabetes), and No. 18 Diovan (for hypertension).

Another six of the top 20 selling drugs in the world are mimics of natural products. No. 6 Abilify (for psychosis and depression), No. 7 Singulair (for asthma), No. 10 Cymbalta (for depression and [anxiety disorders](#)) are

some of the examples.

Although the pharmaceutical industry has made serious efforts to get away from relying on the natural world by attempting to create rationally designed drugs using synthetic compounds, nature-derived drugs still constitute a substantial percentage (26%) of recently approved drugs.

Nature-derived drugs not in every species

The conventional view about nature-derived drugs is that as every nature species produces biologically active molecules, one can find drugs from almost any major block of species groups if one looks and searches for them hard enough.

This view has been proven wrong in a first-ever comprehensive study of the species origins of nature-derived drugs conducted by researchers from the National University of Singapore (NUS) and Tsinghua University. Published in *Proceedings of the National Academy of Sciences* of the United States of America in July 2011, the research showed that drug producing species are concentrated and clustered in a limited number of families.

Data analysed by the research team showed that out of 886 nature-derived drugs discovered in the last 50 years (1961 to 2010), 88% or 783 were from previously known drug producing families. A further 41 were from near neighbours of known productive families. Only 62 came from 'dark horses' that were completely outside of the known clusters.

Lead researcher Professor Chen Yu Zong from the Department of Pharmacy at NUS, said, "In each kingdom of life, the drug-producing families are strongly clustered. Only a limited number of molecular scaffolds are privileged drug-like structure made by specific metabolic genes in certain species families. Some families with lots of bioactive

compounds have never produced a drug because their metabolic genes are not capable of producing privileged drug-like structures, even though they can produce bioactive structures. "

Focus on family members

The findings from this research can now point us to the direction on where to concentrate on the search for new drugs, and that is from pre-existing drug-productive families.

In explaining this rationale, Prof Chen said, "We have identified and highlighted a number of families that have not produced an approved drug but are likely in the drug-producing clusters and potentially produce future approved drugs. Just like by knowing the clustered distribution patterns of oil fields, one knows where to place their bets on the next oil field based on existing findings. For instance, if one finds the first oil-producing well somewhere in the South China seas, by knowing that oil fields tend to be clustered, there is a higher chance in finding the next oil fields by a search of the surrounding areas."

By focusing on pre-existing drug-productive families, resources can be concentrated on manipulating and expanding the families for producing new, as well as existing drugs. In addition, these pre-existing drug-productive families can be studied on why they produce privileged drug-like structures, and the knowledge can be used for designing new and novel drugs.

The potential impact of the research, concludes Prof Chen, is "to promote bioprospecting efforts on those species and species families that are likely to produce new drugs, thus enabling the increase of new drug productivity."

Provided by National University of Singapore

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