From rare bugs to test tube drugs

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(PhysOrg.com) -- Scientists at the University of St Andrews have created exotic biological compounds in a test tube by uncovering some of Nature's chemical secrets.

The development for preparing fluorinated chemicals, an important group of compounds which comprise commercial entities such as Teflon and Prozac, could help the multibillion dollar industry which currently makes the materials by hazardous methods.

The discovery by the researchers in the School of Chemistry demonstrates, for the first time, that fluorinated molecules can be made in the laboratory but under mild biological conditions.

Professor David O'Hagan, who led the team, is excited by the breakthrough. He explained, "Fluorinated chemicals are big in pharmaceutical chemistry, and they also play an important role in medical imaging.

"In a very few organisms, nature has found a way of making these compounds under mild conditions, and we have harnessed that.

"We hope that our biological route can be applied to the synthesis of fluorinated amino acids and sugars and we are now applying the technology to make molecules for medical imaging applications aimed at detecting cancer tumours."

Fluorinated chemicals are important globally in the pharmaceuticals and

agrochemical industries as well as in polymers such as Teflon that is used for non-stick pans, clothing and even buildings.

Other well known compounds in this category include the antidepressant Prozac, the anti fungal treatment diflucan and the cancer chemotherapy agent 5- fluorouracil.

However, these materials are made using noxious fluorination chemicals which present the industrial laboratory with considerable safety and toxicology hazards. The method discovered at St Andrews' Centre for Biomolecular Sciences, is a rare environmentally friendly process for making fluorine chemicals, which operates in water with no particular waste or toxicology hazards.

Professor O'Hagan continued, "Now, the St Andrews' team have uncovered the secrets of how this rare soil bacterium (Streptomyces cattleya) can make a fluorinated amino acid we have put this into action.

"It has been a major goal at St Andrews to discover how the bacteria make these unusual fluorinated compounds. Five biological catalysts (enzymes), including the important fluorinating catalyst (fluorinase), were over-produced by genetic engineering and they have been combined in a test tube. The cocktail has resulted in the successful synthesis of a fluorinated amino acid from the mineral source, fluoride."

As the 13th most abundant element, fluorine is very plentiful on the earths crust. However, it is tied up as insoluble fluoride minerals and the available fluoride in sea and surface water is very low. As a consequence nature has hardly developed a biochemistry of fluorine and there are very few naturally occurring fluorinated compounds. Only two bacteria and a handful of highly poisonous plants have been discovered in Africa and other tropical regions which can make toxic organic fluorine compounds.

The team involved St Andrews University Ph.D students Stuart Cross and Ryan McGlinchey, postdoctoral researcher Dr Hai Deng and a colleague from the Queen's University in Belfast, Dr Jack Hamilton.

The paper "In vitro reconstituted biotransformation of 4-fluorothreonine from fluoride ion: Application of the fluorinase" is published by the *Journal Chemistry & Biology*.

Source: University of St Andrews