Growing corn to treat rare disease

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(Phys.org)—The seeds of greenhouse-grown corn could hold the key to treating a rare, life-threatening childhood genetic disease, according to researchers from Simon Fraser University.

SFU biologist Allison Kermode and her team have been carrying out multidisciplinary research toward developing enzyme therapeutics for lysosomal storage diseases - rare, but devastating childhood genetic diseases – for more than a decade.

In the most severe forms of these inherited diseases, untreated patients die in early childhood because of progressive damage to all organs of the body.

Currently, enzyme treatments are available for only six of the more than 70 diverse types of lysosomal storage diseases.

"In part because mammalian cell cultures have been the system of choice to produce these therapeutics, the enzymes are extremely costly to make, with treatments typically ranging from $300,000 to $500,000 per year for children, with even higher costs for adults," says Kermode, noting the strain on healthcare budgets in Canada and other countries is becoming an issue.

Greenhouse-grown maize may become a platform for making alpha-L-iduronidase, an enzyme used to treat the lysosomal storage disease known as mucopolysaccharidosis I, according to research published in this week's *Nature Communications*.

The findings could ultimately change how these enzyme therapeutics are made, and substantially reduce the costs of treating patients. The novel technology manipulates processes inside the maize seed that "traffick" messenger RNAs to certain parts of the cell as a means of controlling the subsequent sugar processing of the therapeutic protein.

In this way, the researchers have been able to produce the enzyme drug in maize seeds. The product could ultimately be used as a disease therapeutic, although it is still "early days," says Kermode, and several research goals remain to be accomplished before this can become a reality.

Kermode says the success of the work underscores the power of multidisciplinary research that included contributions from SFU chemistry professor David Vocadlo, and from UBC Medical Genetics professor Lorne Clarke. It further underscores the importance of connections between SFU and Australia's Griffith University, through collaborative researchers Mark von Itzstein and Thomas Haselhorst.

"In 2005, we had the basis of our story worked out," says Kermode. "Taking it to the next level involved their precise analyses to determine the sugar residues on the therapeutic enzyme produced by the modified maize seeds.

"When we first looked at the sugar analysis data we were amazed at how well the 'mRNA-trafficking strategy' had worked, and the high fidelity of the process for controlling the sugar-processing of the therapeutic protein. This is critical as sugar processing influences the characteristics of a protein (enzyme) therapeutic, including its safety, quality, half-life in the bloodstream, and efficacy. The work could well extend to forming a platform for the production of other protein therapeutics."

Kermode also credits SFU research associate Xu He, the first author of

the *Nature Communications* paper. Her funding sources included NSERC Strategic grants and a Michael Smith Foundation for Health Research Senior Scholar Award, and in related research, a Canadian Society for Mucopolysaccharide and Related Diseases grant.

More information: www.nature.com/ncomms/journal/ … full/ncomms2070.html

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