Dr Kevin Yueju Wang and his team, from Northeastern State University, focus their research on the sustainable, low-cost production of drugs to treat stroke victims. They are pioneering the use of transgenic plants to produce drugs that dissolve stroke-causing blood clots.

**Planting Seeds of Hope**

**New drug production method could provide affordable, safe treatment for stroke victims**

**Why is it preferable to use plants (rather than mammalian cells) to produce drugs?**

Plants can be grown and maintained at much lower cost than bacteria, yeast or mammalian cells. This means initial studies can be done with a lower financial investment. Additionally, once created, the source (leaves or seeds) is potentially unlimited. They are also preferable to other types of cell in terms of cost, safety and the speed of production. They are able to produce the complex proteins that are required, including antibodies. Unlike mammalian cells, there is also no risk that the drug will become contaminated by animal pathogens, for example viruses. This is a huge boost for the safety of these drugs. Read more: [http://www.ncbi.nlm.nih.gov/pubmed/26633378](http://www.ncbi.nlm.nih.gov/pubmed/26633378)

**Can you give a brief overview of how these plants are genetically modified?**

We identified potential genes (DSPA α1 and tPA) suitable for plant-based protein development. Both genes were synthesised and cloned in a plant gene expression vector. Both genes were driven by seed-specific promoters, which target expressed proteins only in seeds. The tobacco leaf discs will be transformed using the natural genetic engineer, Agrobacterium tumefaciens. The shoot grown from a single cell containing foreign genes will be screened by molecular techniques, and then selected for producing seeds. Proteins from seeds will be extracted and purified. They will then be used to dissolve fibrin and blood clots.

**What are the challenges of using transgenic plants to produce drugs?**

The field of using transgenic plants for pharmaceutical drugs is relatively new, and, as such, there are not many existing protocols for us to follow. Each plant species is made up of unique sets of proteins and metabolites so the purification process is also unique for each species. The complexity of the plant make-up means that designing a purification method (to isolate the proteins produced by the transgenic plant) is very complex. In addition, crops grown in fields (like wheat or rice) raise cross-contamination concerns: the pollen from the transgenic plant may contaminate normal plants that are being grown nearby. Currently, the use of food crops for the production of recombinant pharmaceutical compounds (made using transgenic plants) is restricted. Tobacco is an excellent candidate for pharmaceutical production. It is not a food crop and has a simple gene transfer system. The plants can be produced in just six months and both the leaves and the seeds can be used for production. The systems for ensuring biosafety and the processes for purification have both been established for tobacco. Read more: [http://www.ncbi.nlm.nih.gov/pubmed/26633378](http://www.ncbi.nlm.nih.gov/pubmed/26633378)

**Are there any other natural anticoagulant protein sources that can be used to treat stroke?**

There are currently no effective anticoagulant proteins used to treat stroke. Some thrombolytic agents are available to prevent stroke. These include, among others: streptokinase, secreted by several species of streptococci; urokinase, found naturally in humans, especially in urine; nattokinase from fermented soybeans, a dish known as natto; and lumbrokinase from earthworms. We are working on using plants to produce these anticoagulant proteins.

**How do you plan to develop your research in the future?**

For current tPA or DSPA α1, we are refining the purification process. We expect to produce proteins with 99.99% purity for our pre-clinical safety test. In the future, we will conduct clinical trials and put the proteins into clinic usage. We will discover more candidate genes that meet a commercial need. We will develop a good production system and build a bridge between basic research and its commercial applications.
In comparison to mammalian-based systems, the use of transgenic plants is significantly cheaper and safer, as there is a reduced risk of contaminating the drug with pathogens.