



## ***'Mechanisms underlying improved molecular pharming by protease inhibitors'***

### **PhD position on Molecular Pharming at University of Oxford with Leaf Expression Systems (LES)**

**Description of the project:** Molecular Pharming is a fast-growing new industry in which plants are used to produce vaccines, antibodies, glyco hormones and other pharmaceutical proteins. Thanks to the quick, transient expression of biopharmaceuticals in *Nicotiana benthamiana* leaves by infiltration with *Agrobacterium tumefaciens* (agroinfiltration), there are now companies that are able to produce 10 million influenza vaccines in only 6 weeks. Since early 2017, the UK now has a purpose-built facility based on the Norwich Research Park, called Leaf Expression Systems (LES). LES uses a proprietary plant-based expression platform to prepare a variety of different proteins, including vaccines and antibodies.

Processing and proteolysis by endogenous plant proteases is currently a major obstacle in the agroinfiltration platform. Supported by ERC funding, the VdH laboratory is unravelling the proteolytic machinery of *N. benthamiana* [1], and has recently identified three new, unrelated protease inhibitors (PIs) that boost levels of recombinant proteins (RPs: antibodies, glyco hormones and human enzymes). Co-expression with PIs causes a 10-40 fold increase in RP levels. Interestingly, co-expression of PI combinations increases the RP expression levels even further, indicating that they suppress a proteolytic network that involves proteases from different catalytic classes.

The **AIM OF THIS PROJECT** is to use these PIs in the Molecular Pharming context at LES in Norwich, and to identify the underlying molecular mechanism in the VdH lab in Oxford. This project takes advantage of the extensive toolbox and expertise on proteases in the VdH laboratory and establishes an exciting collaboration with a new industry in the UK.

**Starting date and length:** The position is for four years, starting in October 2018.

**Location:** The project will be mostly in the VdH laboratory at the Department of Plant Sciences in Oxford, in close collaboration with scientists at LES in Norwich. There is a placement of 3 months in the first year at LES to test the PIs under industrial conditions.

**Funding:** The PhD position is funded for four years by the Industrial Collaborative Awards in Science and Engineering (iCASE) of the BBSRC and is embedded in the Doctoral Training Centre (DTC) in Oxford.

**Applicant profile:** Applicants should be from the UK (or UK resident for >3 years), have a university degree in biology or a related subject, and highly motivated to do a PhD on Molecular Pharming in an interdisciplinary research team. Experience with protein work and molecular cloning are strongly desired.

**Application:** You can submit your application to Professor Renier van der Hoorn before December 31 2017. Please email a strong motivation letter stating why this is an interesting topic and why you have the right attitude and expertise to make progress in this field. Also send your CV and names of three references.

**More information:** Please see [www.plantchemetics.org](http://www.plantchemetics.org) for more information and contact [renier.vanderhoorn@plants.ox.ac.uk](mailto:renier.vanderhoorn@plants.ox.ac.uk) for more details.

**Reference:** [1] Grosse-Holz F, Kelly S, Blaskowski S, Kaschani F, Kaiser M, Van der Hoorn RAL (2017) The transcriptome, extracellular proteome and active secretome of agroinfiltrated *N. benthamiana* uncover a large, diverse protease repertoire. **Plant Biotechnol. J.** *in press* PMID29055088

