High Value Biorenewables – Proof of Concept Call 1

Development of a new biocatalytic process to generate high value chemicals from lignin	
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Company:	**Novozymes A/S**

Lignin is a polyphenolic polymer that is a major structural component of plant secondary cell walls. It is the most abundant aromatic polymer in nature and has considerable potential as a sustainable source of valuable aromatic compounds that can replace fossil fuels. Recently, the flavone tricin was found to be a significant component of monocot lignin, such as that found in the secondary cell walls of wheat and rice. As tricin is a potentially valuable chemical there is significant interest in finding methods of extracting tricin from lignin. To date no efficient and economical way of isolating tricin has been found. Tricin has been reported to possess a range of pharmaceutical attributes, including anti-oxidant, anti-inflammatory and anti-aging properties. It has also been shown to have an immune-modulatory effect on macrophages and to be active against *Leishmania infantum*, the causative organism of leishmaniasis, but its current expense prevents any further in depth investigations.

Hundreds of millions of tons of agricultural residues are burnt in the field or discarded, which has negative impacts on the environment and wasting a potentially valuable resource. We are interested in investigating how microbes deconstruct these residues, with a focus on identifying new enzymes that can potentially valorise lignin. We have recently discovered a new ligninase from the soft rot fungus *Graphium* sp. that cleaves β-O-4 linkages in lignin, the aim of this project is to fully characterise the degradation products of lignin which includes tricin and establish a new method for the preparation of tricin from crop residues.

Producing Hyaluronic Acid in Acetobacter species	
Lead applicant's name:	**Professor Tom Ellis**
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Co-applicant's name:	**Dr Vivianne Goosens**
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Industry partners:	**Dr Ben Reeve**
Position held:	**CTO**
University/ research institute:	**Puraffinity**

Hyaluronic acid (HA) is a polysaccharide used in medical and cosmetic applications totalling a billiondollar industry. In humans, HA forms an intercellular matrix associated with protection against aging and cancer. Historically, rooster combs provided the industrial source of HA, however as pathogenic bacteria produce HA to 'hide' from the immune system, industry now uses these: with bacterial Hyaluronic Acid Synthase (HAS) systems producing animal-free HA. These *Streptococcus*-based biosynthesis methods have accelerated HA production, but manufacturing is hampered by bacterial endotoxins. High molecular weight HA is also desired but to generate longer chain lengths with *Streptococcus* requires expensive media supplementation. While most organisms do not innately secrete massive amounts of polysaccharides, *Acetobacter* species do, producing large yields of bacterial cellulose (BC). BC is produced cheaply at scale from these bacteria with low immunogenicity. Indeed, BC is routinely used in surgical implants. Importantly, due to the immense innate supply of glucose and UDP in BC-producing bacteria, these cells have the metabolic propensity to secrete long chains of sugars without supplementation. *Acetobacter* thus offer great potential as polysaccharide biosynthesis workhorses. Our team consists of a synthetic biologist with extensive tools and experience for engineering the Acetobacter *Komagataeibacter rhaeticus* and an industrial partner, Puraffinity, with a historic interest in industrial HA production. Together we are in the unique position to develop *K. rhaeticus* into a novel bacterial HA-production workhorse that, due to its native metabolism, would produce high valued long-chained HA from agroindustrial waste, in an animal free, and endotoxin-free manner.