國立嘉義大學九十五學年度

生物科技研究所碩士班招生考試試題

科目：專業英文

1. Translation from English to Chinese. (30%)

An ambitious biotechnology programme carried out over the past four years by Ken Gruysand colleagues, to produce plants that are able to synthesize a commercially useful plastic, poly-hydroxybutyrate-co-valerate (PHB/V), has been successfully completed recently. The plant-derived co-polymer has similar properties to the plastics used in shampoo bottles and disposable plastic razors, with the distinct advantage of being biodegradable. The environmental benefit of biodegradability is obvious but the renewable nature of this plastic is perhaps more important. The plants use photosynthetically fixed CO_2 and water to make the plastic, which after use and disposal is degraded back to CO_2 and water, which is used by the plant to make the plastic - a fine example of a virtuous circle. Oil is a limited global resource but the size and efficiency of the world's oil industry makes it the second cheapest bulk liquid on Earth after un-purified sea water. This means that petrochemically derived plastics are relatively inexpensive. However, the environmental consequences of oil production, plastics manufacturing, the 'hide and forget' disposal of plastics and the use of a non-renewable resource have recently increased the desirability for a 'green' alternative. Any alternative must be economic in comparison to oil-derived plastics if it is to succeed in the world marketplace. In addition, plastic from an alternative source must have similar physical and chemical properties to its oil-based competitors.

Although low levels of a natural PHB polymer have been detected in plants and in other eukaryotes, the biosynthetic pathway is uncharacterized and the PHB is of a low molecular weight. Significant PHB production in transgenic *Arabidopsis* was first demonstrated in 1994 by Chris Somerville's group. This was achieved by introducing all three bacterial gene products (phbA, B and C) into the plastid via the N-terminal addition of the small sub-unit RUBISCO-targeting peptide. Their achievement was ground breaking, producing one transgenic plant with 14% dry weight PHB in its leaves. However, production of the PHB/V co-polymer required further metabolic engineering.

The research impetus could now shift to the problem of producing the co-polymer, which required the additional presence of C5 carbon units (poly-hydroxyvalerate, PHV) in the polymer. The team recognized that these could be derived from endogenous acetyl CoA and propionyl CoA, but the concentration of free propionyl CoA in plants is low. It was necessary to redirect intermediates of metabolism to provide a pool for PHV biosynthesis. The team studied the pyruvate dehydrogenase (PDH) complex from oilseed rape, which normally produces acetyl CoA from pyruvate for lipid biosynthesis. They showed that it is capable of converting an intermediate in isoleucine biosynthesis, 2-ketobutyrate, into propionyl CoA, albeit at a less efficient rate. The group's approach to increasing the levels of available 2-ketobutyrate was to increase the flux through the whole pathway. The key enzyme that limits the flux of the isoleucine pathway, threonine deaminase, is negatively regulated by isoleucine.

2. Translation from English to Chinese. (20%)

Along with disease, drought, and pests, metals are a key enemy of plant growth. Aluminum, for example, the most abundant metal in Earth's crust, is normally locked up in minerals. But in acid soils, like those of the south-eastern United States, Central and South America, North Africa, and parts of India and China, aluminum is set free as ions that poison plant roots, probably by making the cells rigid and unable to lengthen. The result is stunted plants and poor harvests, a problem on up to12% of soils under cultivation worldwide. For decades, plant breeders coped with metals in soils by crossing metal-sensitive plant varieties with the few species that thrive despite their presence. But tolerant crops are few, and classical plant breeding is slow because crop genomes are large and complex. Lately, however, crop researchers have turned to genetic engineering to improve traits ranging from pest resistance to nutritional value and now they are taking the first steps toward producing metal-tolerant plants as well. Within the last year, several research groups have identified metal-resistance genes, or their approximate locations, in mutant plants and other organisms. In some cases, they have gone on to identify the enzymes made by the genes, which help cells cope with metals by excluding them, sequestering them within the cell, or transforming them into volatile forms that can escape to the air. "This recent work is exciting," says plant biochemist Himadri Pakrasi of Washington University in St. Louis. Now we have mechanisms for coping with toxic metals and the possibility of inserting them into crops to boost their growth.

3. After reading the following abstract, please describe briefly how Tau protein induces neuronal death. (25%)

The altered function and/or structure of Tau protein is postulated to cause cell death in tauopathies and Alzheimer’s disease. However, the mechanisms by which Tau induces neuronal death remain unclear. Here we show that overexpression of human tau and of some of its N-terminal fragments in primary neuronal cultures leads to an *N*-methyl-D-aspartate receptor (NMDAR)-mediated and caspase-independent cell death. Death signaling likely originates from stimulation of extrasynaptic NR2B-subunit-containing NMDARs because it is accompanied by dephosphorylation of cAMP-response-element-binding protein (CREB) and it is inhibited by ifenprodil. Interestingly, activation of NMDAR leads to a crucial, sustained, and delayed phosphorylation of extracellular-regulated kinases 1 and 2, whose inhibition largely prevents

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tau-induced neuronal death. Moreover, NMDAR involvement causes the fatal activation of calpain, which, in turn, degrades tau protein into a 17-kDa peptide and possibly other highly toxic N-terminal peptides. Some of these peptides are hypothesized, on the basis of our *in vitro* experiments, to initiate a negative loop, ultimately leading to cell death. Thus, inhibition of calpain largely prevents tau degradation and cell death. Our findings unravel a cellular mechanism linking tau toxicity to NMDAR activation and might be relevant to Alzheimer's disease and tauopathies where NMDAR-mediated toxicity is postulated to play a pivotal role. (*Amadoro G et al., PNAS, 103: 2892-2897, 2006*)

4. After reading the following abstract, please describe briefly how SOCS1 inhibits tumor necrosis factor. (25%)

We have previously shown that ASK1 undergoes ubiquitination and degradation in resting endothelial cells (EC) and that proinflammatory cytokine tumor necrosis factor (TNF) induces deubiquitination and stabilization, leading to ASK1 activation. However, the mechanism for the regulation of ASK1 stability is not known. In the present study, we have shown that SOCS1, a member of suppressor of cytokine signaling, induces ASK1 degradation. SOCS1 was constitutively expressed in EC and formed a labile complex with ASK1 that can be stabilized by proteasomal inhibitors. The phosphotyrosine-binding SH2 domain of SOCS1 was critical for its association with ASK1. Thus a SOCS1 mutant defective in phosphotyrosine binding failed to bind to and induce ASK1 degradation. Phosphotyrosine of ASK1 was induced in response to growth factors, and TNF induced dephosphorylation and dissociation of ASK1 from SOCS1. ASK1 with a mutation at Tyr-718 diminished the binding to SOCS1, suggesting that the phosphotyrosine-718 of ASK1 is critical for SOCS1 binding. Moreover, ASK1 expression and activity were up-regulated in SOCS1-deficient mice and derived EC, resulting in enhanced TNF-induced activation of JNK, expression of proinflammatory molecules, and apoptotic responses. We concluded that SOCS1 functions as a negative regulator in TNF-induced inflammation in EC, in part, by inducing ASK1 degradation. *(He Y et al., J. Biol. Chem. 281: 5559-5566, 2006)*