

## 第一部分 簡答題 (60%)

1. 請解釋 DNA array 之原理並概述其操作過程(10%)。請舉例說明其應用實例(10%)。
2. 去年之諾貝爾生物醫學獎項頒給了三位研究 telomere 的科學家，請概述其研究之內容及重要性(10%)。
3. 請解釋下文之大意(10%)，並請以您細胞學之知識，猜測本文中所使用之實驗技術(10%)並解釋該項實驗技術之原理(10%)。

Dr Joerg Hartkamp and Dr Stefan Roberts have found that the protease HtrA2 can “clean” cells of the oncogene WT1, which is found at high levels in many leukaemias and solid cancers such as breast and lung cancer.

Their work has given drug designers a new target which will allow them to develop treatments for all these cancers in which WT1 expression is elevated.

WT1 is a well-known factor in cancer, having been discovered 20 years ago. It suppresses the development of Wilms’ tumour of the kidney, a rare cancer that affects one in 10,000 children. However it has a cancer causing role in other forms of the disease, particularly leukemias such as acute myeloid leukaemia (AML) and chronic myeloid leukaemia (CML).

This latest study – published in the journal Molecular Cell and funded by the Wellcome Trust, Cancer Research UK and the Association of International Cancer Research (AICR) – is the first to identify the enzyme that can rid cells of WT1.

Dr Hartkamp, at the University of Manchester’s Faculty of Life Sciences, said: “The cancer causing role of WT1 has been known for many years, but how it worked was not understood so we studied a regulatory domain of WT1 to see what modified its activity. We carried out a fishing experiment and discovered the role of the protease HtrA2 instead, by accident. This discovery has a much bigger impact.

“We have filled in the black box of WT1. It is this protease that is doing the trick – it can clean cells of WT1.”

Dr Roberts, who initiated the work at Manchester and is now at the University at Buffalo, added: “There are great prognostic implications in leukaemias but this protease may have even more targets. It is unlikely that a protease cleaves only one transcription factor such as WT1.”

AICR’s Scientific Adviser Dr Mark Matfield said: “This exciting new finding shows why it is so important to carry out basic research into cancer. More and more these days, we see basic

research discovering something unexpected about cancer that could be a major new step forward. The more we find out about cancer the closer we get to beating it.”

It is hoped that patients will be screened for a high level of WT1 and, if this is the case, clinicians can reactivate HtrA2. And as WT1 expression is low in healthy adults, oncogenic expression of WT1 has been found to be tumour specific so targeting WT1 will be less damaging to the patient’s general health.

第二部份 解釋名詞(40%)

1. FRET
2. GPCR
3. GFP
4. lipid raft
5. proto-oncogene
6. unfolded protein response
7. N-myristoylation
8. Tumor suppressor genes
9. Autophagy
10. Cohesin

