Venue: GIZA
21st August 2007
1130-1245 hr

Symposium 1C: New paradigms in anti-infective therapy

S1C-1. RNA Interference – The role of siRNAs as alternative therapeutic agents

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A newly described function of ribonucleic acid (RNA) in regulating cellular gene expression in both animal and plant cells exceeds its task as a simple transcript of genetic information and it reveals another important role of this physiologically versatile primordial biopolymer. Two classes of small double stranded RNAs, small inhibitory RNA (siRNA) and microRNA (miRNA), emerge as powerful post-transcriptional and translational regulators of gene expression, respectively, via a mechanism described as RNA interference or gene silencing. Apart from being commonly utilised by plants as a natural defence mechanism against plant viruses, RNA interference is seen as a very valuable approach to antiviral therapies against medically important viruses. In this regard, the focus of this presentation will be on the potential usage of RNA interference as an alternative therapeutic procedure to treating infections with flaviviruses. In addition, a comparison with conventional intracellular antiviral pathways that are naturally functional in animal cells, such as those controlled by interferon type I and dsRNA, will be presented and discussed. The model virus used in this study was West Nile encephalitis virus, a laboratory strain Sarafend, while experimental models were established cell lines, Vero and L929, as well as primary peritoneal macrophages derived from Flavivirus susceptible and congenic resistant mice. The major finding that, under particular circumstances RNA interference may provide a more powerful protection from Flavivirus infection than the standard interferon type I antiviral pathway(s), warrants further research into antiviral effects of RNA interference and development of more standardised approaches to antiviral therapies using siRNA and miRNA.

S1C-2. Nanotechnology in early disease detection and diagnostics

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Diagnostics that detect diseases such as cancer at an early stage, when the disease is most responsive to contemporary therapies, provide the greatest social and economic benefits to society[1]. This has been demonstrated in early disease detection programs such as the PAP smear cervical cancer test and colonoscopy for colon cancer. Unfortunately, current diagnostic protocols typically depend on a complicated variety of tests based on a wide range of different, and often expensive, technological platforms. Each different platform requires significant investment in single-use equipment and training. Despite this investment, results can be ambiguous and require multiple, different tests to produce a confirmed result for a single pathogen. Nanotechnology offers the promise of miniaturized, inexpensive, flexible and robust "plug-and-play" molecular reading systems which can be effectively deployed in the field. In this talk we will present several platforms which our Centre is currently developing for such applications.

Biomarkers are novel biological markers which distinguish the characteristics of diseased cells. To date, the leading tool in proteomics for biomarker detection is mass spectrometry (MS). However MS has a limited capacity to identify and quantify proteins in complex mixtures where most of the

known blood borne biomarkers occur at very low abundance and are therefore seldom revealed. The lack of tools available to date has meant that research efforts have proceeded slowly. We shall present an alternative method, developed within our Centre[2-8], of screening for disease biomarkers on extremely cheap platforms: encoded colloidal suspensions. The colloidal suspensions are produced via combinatorial chemistry procedures, however are optically encoded for rapid and unique recognition of each individual compound. A unique feature of the technology is the ability to challenge complex biological mixtures (eg. blood sera) with libraries of binding motifs (such as peptides or DNA) attached to particles which have been optically bar-coded and can be screened by high-throughput methods such as flow cytometry.

1) Hartwell et al, Nature Biotech. 24 (2006); Etzioni et al., Nature Revs., Cancer, 3 (2003). **2,3)** Corrie et al., Langmuir, 22, 2731 (2006); Johnston *et al*. Chem. Comm. 848 (2005). **4, 5)** Lawrie *et al*. Applied Nanoscience, 1, 1, (2004); Adv. Functional Materials 13(11) 887 (2003). **6)** Battersby *et al*. Chem. Comm. 14, 1435 (2002); **7)** Trau, Battersby, Adv. Materials, 13, 975 (2001); **8)** Battersby, Lawrie, Trau, Drug Discovery Today, 6, 123 (2001); **9)** Trau *et al.,* J. Am. Chem. Soc. 122, 2138 (2000).

S1C-3. Turning the tables on quorum sensing – autoinducers of quorum sensing as targets for infection control

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Many bacterial pathogens have adopted a cell-cell communication mechanism known as quorum sensing to coordinate microbial activities essential for infection and survival in host. These quorum sensing pathogens produce, detect, and respond in a population-density-dependent manner to specific small signal molecules in synchronizing expression of virulence genes among local family members. This sophisticated community genetic regulatory mechanism may facilitate bacterial infections by allowing pathogens to mount their attack to overcome host defense mechanisms. In addition, quorum sensing is also known to regulate other bacterial functions important for environmental competence and survival fitness, such as biofilm formation and antibiotic resistance. However, this clever quorum sensing mechanism has its loopholes that can be targeted for prevention and control of microbial infections. By focusing on the research progresses in my laboratory, this talk will discuss our current understanding of the roles of quorum sensing in microbial physiology, the scope of quorum sensing regulation, the feasibility and the potentials of quorum quenching approaches in infection control, and the future opportunities and challenges in investigation of quorum sensing and in prevention and control of infectious diseases.