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# Targeting transcription factors with DNA interactive small molecules

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Transcription factors are regulatory macromolecules that induce profound and sustained effects in cells by interacting with, and modulating the expression of genes responsible for critical cellular processes. Interaction of a small molecule with the consensus DNA sequence can prevent a transcription factor from recognizing its cognate sequence, thereby preventing expression of genes associated with the transcription factor. Transcription factor inhibition is an exciting new area of drug discovery, and is considered by some experts to represent the "next wave" of cancer therapeutics following the kinase inhibitors (which have now reached maturity) and the antibody-based approaches which are now in the ascendancy. There are few approved drugs at present that work by selectively inhibiting transcription factors, and so there is significant clinical and commercial potential. From a scientific/clinical perspective, this approach has the advantage that a selective and potent inhibitor would act at the ultimate signalling point of gene expression (i.e., the promoter region of a gene) thus directly modulating the expression of genes carrying the cognate DNA recognition site of the targeted transcription factor. Furthermore, there are sub-families of transcription factors (e.g., STAT1 and STAT3), and it may prove possible to target these independently, thus achieving fine-control over transcription. This is an important distinction from the kinase inhibitors that also modulate gene expression, but have multi-pathway downstream targets and are rarely highly selective, as their kinase target will usually control a range of transcription factors. The talk will explore innovative DNA targeting therapeutic approaches to develop low molecular weight "druggable" molecules that can be targeted to unique transcription factor recognition sites in the human genome. Various mechanisms can be used including the inhibition of protein-protein interactions (PPIs) and protein-DNA interaction (PDIs). A number of duplex-DNA and promoter G- Quadruplex-binding agents are being developed to target the PDI interaction, and some examples will be presented.

## Biography

Khondaker Miraz Rahman graduated as a pharmacist from the Faculty of Pharmacy of University of Dhaka, Bangladesh in 1996. He worked for 3 years as a research and development pharmacist at SK&F Pharmaceutical before moving to academia in April 2001 and joined the Pharmacy department of University of Asia Pacific as a Lecturer. In October 2003, he was appointed as a Lecturer in pharmaceutical chemistry at Dhaka University and was promoted to Assistant Professor in June 2005. He completed his PhD research at the London School of Pharmacy (now UCL School of Pharmacy) under the supervision of Professor David Thurston. He joined the CRUK Protein-Protein Interaction Research Group as a CRUK Research Fellow in July 2009. He was appointed as a Lecturer in Medicinal Chemistry at King's College in May 2012. He has published over 35 peer-reviewed articles in leading journals and presented over 30 posters/talks at various international conferences.

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