RESEARCH FRONT

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Foreword

Nucleic Acids

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Functional nucleic acid-based therapeutic technologies have attracted significant interest in recent years for targeting the underlying molecular pathogenesis of various diseases. Some of the prominent synthetic functional nucleic acids are antisense oligonucleotides (AOs), short-interfering RNA (siRNA), DNAzymes and microRNA-targeting oligonucleotides (antimiRs), which have proven to be very efficient in cleaving, blocking or repairing pathogenic RNAs. In 2006, a Nobel prize was awarded for the discovery of siRNA-mediated gene silencing technologies, which brought the nucleic acids field further into the spotlight. Nucleic acid aptamers are another important class of short synthetic functional nucleic acids that can bind to a specific molecular target with very high affinity and specificity because of their ability to adopt three-dimensional shapes in solution. Aptamers, often called 'chemical antibodies' are ideal molecules for targeted drug delivery, therapy, and molecular imaging, and for use as biosensors. Therapeutic nucleic acids and other drug molecules can be conjugated to aptamers to achieve tissue-specific delivery.

Functional nucleic acids composed of naturally occurring nucleotide monomers are not suitable for therapeutic development mainly because of their low nuclease resistance, poor (mismatch) recognition capabilities, and decreased target binding affinity to complementary RNA or DNA. To circumvent these issues, chemically modified nucleic acid analogues are generally used to construct functional nucleic acid sequences in combination with their natural counterparts or as fully modified variants. Several chemically modified nucleic acid analogues have been developed in recent years. So far, three oligonucleotide drug candidates have been approved by the United States Food and Drug Administration (US FDA) for clinical use, including Vitravene, a 21-mer phosphorothioate-modified AO for the treatment of cytomegalovirus retinitis; Macugen, a 27-mer aptamer oligonucleotide modified with 2′-*O*-methyl and 2′-Fluoro RNA nucleotides for the treatment of age-related macular degeneration; and Kynamro, another AO modified with 2′-*O*-methoxyethyl-RNA chimera for the treatment of familial hypercholesterolemia. Recently, another chemically modified AO candidate developed in Australia, eteplirsen, entered Phase-3 clinical trials for the treatment of Duchenne muscular dystrophy; it is presently awaiting a US FDA decision. Several other therapeutic oligonucleotide candidates are currently in various stages of clinical and pre-clinical investigation.

To highlight recent developments in this field with the goal of expanding research on functional nucleic acid technologies in Australia, the first international symposium on 'Functional Nucleic Acids: From Laboratory to Targeted Molecular Therapy' was organised and held at Murdoch University, Perth, Australia, from 26 to 27 November 2015. This successful event attracted international experts from Australia, Denmark, Belgium, Canada, Japan, India, Sweden, and New Zealand. The conference covered all aspects of functional nucleic acid-based technologies, including novel chemically modified nucleotides, therapeutic applications of novel nucleic acid analogues, drug delivery, and targeted therapy using nucleic acid aptamers, from which this Nucleic Acids research front for the *Australian Journal of Chemistry* was derived. Five papers have been selected for this research front by following a strict peer-review process. P. Nielsen and colleagues describe the development of novel double-headed nucleotides as building blocks for constructing new nucleic acid architectures,[1] while R. Baker and his team highlight the therapeutic potential of miR-494 in thrombosis and other diseases.[2] M. Kuwahara and co-workers discuss the non-equilibrium capillary electrophoresis separation and selection of a long DNA aptamer,[3] and J. R. Kanwar and colleagues demonstrate E-cadherin aptamer conjugated delivery of doxorubicin for targeted inhibition of prostate cancer

Rakesh N. Veedu obtained his Ph.D. degree in synthetic organic chemistry in 2006 from The University of Queensland, Australia, after completing his M.Sc. studies at Griffith University, Australia. He then continued his post-doctoral career at the Nucleic Acid Center, University of Southern Denmark, in the field of nucleic acid chemical biology. Dr Veedu returned to The University of Queensland in mid-2010 and established an independent research group focussed on developing target-specific therapy using various nucleic acid-based technologies. He is currently a McCusker Fellow and Group Leader at the Centre for Comparative Genomics and Western Australian Neuroscience Research Institute, Murdoch University, Perth, Australia. Dr Veedu's research is focussed on novel functional nucleic acid-based technologies for the development of target-specific therapies to treat various diseases, including solid cancers, neurological diseases, and inherited/genetic disorders. Specifically, his research involves the development, synthesis chemistries, and applications of nucleic acid aptamers, antisense oligonucleotides, siRNA, antimiRs, DNAzymes, and molecular beacons.

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cells.[4] Finally, K. J. Thurecht and colleagues describe the preclinical imaging of siRNA delivery.[5]

As guest editor of this research front, I would like to thank all authors for their wonderful contributions and all reviewers for their efforts in ensuring that the papers are of high quality. I extend my sincere gratitude to Professor Curt Wentrup, former editor-in-chief of the *Australian Journal of Chemistry*, who recognised the importance of nucleic acid chemistry and generously offered to publish this research front. I would also like to thank the current editors-in-chief and the editorial team for their wonderful support. I firmly believe that this research front will help readers of this Journal to gain more insights and benefit from their research into novel nucleic acid-based technologies.

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