International Society on Aptamers

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EDITORIAL

Welcome to the 2020 first issue of INSOAP times, your source to what's happening in the aptamer world presented by the INSOAP team. I usually start these editorials off with a look ahead to the conference and a hope that you've all had a good start to the year. For me personally, it feels as though the bad news hasn't stopped. We've had bush fires decimating the land and reducing some wild life populations to close to extinction. I have gone from watching the hourly updates of fires to hourly updates of Covid-19. For someone that teaches emerging infectious diseases, this is truly a surreal time. There has been devastation across practically every country, and it would be remiss of me not to mention what we are going through. I hope that you are remaining safe, sane, and healthy. I also pass on my condolences to all that have mourned a death. It is going to be a long road to recovery, and while we will get through this, we will have lost a great deal in the process. I am encouraged by the speed at which the scientific world is answering so many questions and I take comfort in knowing that this is going to be the quickest we have ever moved in all areas of research.

While everything has slowed down in the world around us, we have still been working on various initiatives within the Society, and keeping track of what's been going on in the aptamer world and what's being published. You will see all our familiar topics in the following pages. And while we didn't have the Aptamer Symposium in April, we are working on some options. Please make sure you are on the mailing list for INSOAP so we can keep you up to date with this.

As a final note, have you liked our Facebook page? We are currently providing links to new aptamer research papers on a daily basis. Don't have time to keep up to date on current literature? Get our daily updates in your morning newsfeed at https://www.facebook.com/AptaSoc/. Please don't forget to also follow us on twitter (@Aptamer Society, @Japtamers).

Please look after yourselves and those around you. I'll leave you with my favourite quote,

'*May the insanity of others float like clouds beneath your feet*'

Dr Sarah Shigdar
INSOAP President

Inside this issue:

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Keep in touch

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The rise of oligonucleotide therapeutics: good news for the aptamer field!

Lucia Wang, McGill University, Canada

As many of the members of INSOAP know, the use of aptamers as therapeutics is an ongoing challenge. While Pegaptanib, an RNA aptamer that binds and deactivates VEGF to treat age-related macular degeneration, has been on the market for nearly 15 years[1], challenges with oligonucleotide delivery and stability has generally hindered the use of aptamers in the clinic. Over these same 15 years our knowledge about gene expression mechanisms involving antisense oligonucleotides (ASO), RNA interference (RNAi), etc. has grown exponentially, garnering interest in terms of clinical applications.[1] The first oligonucleotide therapeutic to hit the market was an ASO, approved in 1998, for the treatment of cytomegalovirus retinitis. While no longer on the market as better treatments have been developed, it forecasted future interest in oligonucleotide therapeutics.[1] Now, with 10 approved drugs and approximately 100 ongoing clinical trials, therapeutic oligonucleotides are rapidly gaining notoriety in terms of their unique abilities to selectively activate or inactivate proteins that are considered "undruggable" by small molecule and protein-based therapeutics.[2]

Oligonucleotide-based therapeutics are well suited for diseases with a known therapeutic target such as Huntington's disease and amyotrophic lateral sclerosis, among others. Within this family of therapeutics, ASOs and RNAi provide several ways to modify gene expression, either by blocking translation, altering stability, modifying splicing, or eliciting degradation pathways all with the same end goal of altering the expression of the target mRNA. With the high level of selectivity that can be achieved, these drugs can be used fairly safely with limited off-target effects.[1] More specifically, ASOs can have long-term effects, in the order of months, while maintaining reversibility as effects could be reversed simply by stopping treatment. That said, if irreversible treatment is desired, RNAi therapeutics are a great option.[1] Of course, in this case, more stringent testing might be required since, once the drug has been administered, there would be no turning back. Regardless of the specific type of oligonucleotide therapy, they are highly desirable in a clinical setting because their efficacy and safety profile are defined by their sequence and chemical design, so once one therapeutic is created and approved, it would be much easier to rapidly develop related drugs to target other genes associated with the same disease in the same tissue.[3]

With this rising popularity of the field, oligonucleotide therapies are now being considered for a wide variety of diseases. For example, Givlaari is one of the newest FDA approved oligonucleotide drugs for the treatment of acute hepatic porphyria, and Inclisiran, an siRNA-based cholesterol-lowering drug, is months away from FDA approval.[2] The approval of these two new therapies represent the treatment potential that remains to be unlocked with oligonucleotides, particularly since they can address symptoms and diseases where current front-line medications fail. The successes that have been achieved with ASOs and RNAi treatments now puts us at the frontier for novel oligonucleotide therapeutics. This is good news for aptamers! Of course, much work still needs to be done to tackle the challenges that continue to hinder the widespread use, namely drug safety and delivery. However, with the technological developments that have now addressed the previous problems with large-scale manufacturing and allowed for chemical modifications to be made with greater ease, it is likely that more and more oligonucleotide therapies will come into existence in the near future, and hopefully enable new aptamer based candidates as well.

References

1. Scoles, D. R., & Pulst, S. M. (2018). Oligonucleotide therapeutics in neurodegenerative diseases. *RNA Biology*, *15*(6), 707-714.
2. RNAi scores big wins. (2020). *Nature Biotechnology*, *38*(4), 4.

From the Editor

If you have anything you would like to see in the next issue of the INSOAP newsletter, send it directly to sarah.shigdar@deakin.edu.au.

Aptamers Journal

We announced the official journal of INSOAP at Aptamers 2017. Please email us at aptasoc@gmail.com to express your interest in joining the editorial or reviewer team. Please see http://JAptamers.co.uk to submit your article.

3. Khvorova, A., & Watts, J. K. (2017). The chemical evolution of oligonucleotide therapies of clinical utility. *Nature biotechnology*, *35*(3), 238.
4. Levin, A. A. (2019). Treating disease at the RNA level with oligonucleotides. *New England Journal of Medicine*, *380*(1), 57-70.

INSOAP updated list of recently published aptamers

Maureen McKeague, McGill University, Canada

Here are newly reported aptamers since our last issue (August 2019). We only report aptamers that have been characterized with a dissociation constant (Table 1). Typically, we make use of Pubmed to identify newly published aptamers with the keywords “aptamer” and “SELEX”. If we have missed any newly reported aptamers, please let us know (maureen.mckeague@mcgill.ca). Readers should consult the literature (link provided) for verification and further information.

Table 1: Newly-reported aptamers published since our last issue.

Link	Target	Nucleic acid type
https://www.ncbi.nlm.nih.gov/pubmed/31357315	riboflavin	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31357131	fibroblast growth factor receptor (FGFR)	RNA
https://www.ncbi.nlm.nih.gov/pubmed/31369705	wild type and mutated c-KIT receptor tyrosine kinases	RNA
https://www.ncbi.nlm.nih.gov/pubmed/31499431	tacrolimus	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31560515	HIV-1 integrase	DNA (modified)
https://www.ncbi.nlm.nih.gov/pubmed/31563315	*Lactobacillus casei*	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31580650	thrombin; human serum albumin	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31625087	tobramycin	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31636432	sulforhodamine B dyes (Gemini-561)	RNA
https://www.ncbi.nlm.nih.gov/pubmed/31726389	CD63 Protein	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31733056	DNMT1	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31754797	dedicator of cytokinesis 8 (DOCK8) gene	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31757698	penicillin binding proteins (PBP2a)	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31809034	paramylon	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31815219	estradiol, progesterone, testosterone	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31816738	histamine	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31837967	*E. coli* (KCTC 2571)	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31868873	H1N1 virus	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31892242	nonylphenol	DNA
https://www.ncbi.nlm.nih.gov/pubmed/31953175	SipA protein (*Salmonella enteritidis*)	DNA
https://www.ncbi.nlm.nih.gov/pubmed/32020675	DUX4 protein	DNA
https://www.ncbi.nlm.nih.gov/pubmed/32029106	azlocillin	DNA
https://www.ncbi.nlm.nih.gov/pubmed/32038731	interleukin-5	DNA
https://www.ncbi.nlm.nih.gov/pubmed/32050451	di(2-ethylhexyl) phthalate (DEHP)	DNA
https://www.ncbi.nlm.nih.gov/pubmed/32127399	toxic dimer of amyloid β42	RNA
https://www. ncbi.nlm.nih.gov/pubmed/32148021	vimentin	DNA
https://www.ncbi.nlm.nih.gov/pubmed/32155319	toxin B	DNA
https://www.ncbi.nlm.nih.gov/pubmed/32161119	kainate receptor	RNA

https://www.ncbi.nlm.nih.gov/pubmed/32161798	thrombin and TGFb1	RNA
https://www.ncbi.nlm.nih.gov/pubmed/32180322	Human Vascular Endothelial Growth Factor 165	DNA
https://www.ncbi.nlm.nih.gov/pubmed/32210057	1,1,1-trichloro-2-(p-chlorophenyl)-2-(o-chlorophenyl) ethane (o,p'-DDT)	DNA
https://www.ncbi.nlm.nih.gov/pubmed/32222697	MDA-MB-231 (Triple-negative breast cancer)	2'-fluoropyrimidine-RNA

Aptamers, crypto-aptamers and pseudo-aptamers

Alex Kopylov, Moscow State University, Russia

Recently, in connection with the expansion of the fields of research and the application of aptamers, the need has been raised for an exact definition of the concept of “aptamers”. This is required for an adequate use of terms and exchange of information, as well as a qualitative assessment of research results.

In the classic version, an “aptamer” is an oligonucleotide that has high affinity and specificity for the target due to the unique three-dimensional structure, which either pre-exists or is formed upon interaction with the target. In the classic version, aptamers are selected to a specific target from combinatorial oligonucleotide libraries (SELEX). Libraries are giant mixtures of oligonucleotides with a huge variety of nucleotide sequences (more than 1010) to provide the greatest variety of three-dimensional structures. Selection is performed by repeated cycles of the selection stages.
The active development of aptamer studies has led to the appearance of oligonucleotides that are not aptamers in the classical sense of the term, but for which the term “aptamer” is used by inertia. For these oligonucleotides, it is necessary either to modify the term “aptamer” or to introduce a new term. The following modifications of the term “aptamer” are proposed for two new types of oligonucleotides.

Crypto-aptamers (cryptic aptamers). There are oligonucleotides that bind to (or act on) specific cells; however, the molecular target, with which they interact, is unknown. For example, these oligonucleotides are some G-quadruplex DNAs that have antiproliferative activity. Another example is oligonucleotides selected during SELEX for living cells, which have high affinity and specificity for the target cells (they could even change cell functioning); the exact target has not been proven, but only assumed. For example, oligonucleotides selected for cells with high receptor copy number on the cell surface. For these oligonucleotides the term "crypto-aptamers" could be coined; the first part of the compound word "crypto" comes from the Greek "kryptos" in the meaning of "hidden".

Pseudo-aptamers. Often, as a result of SELEX, families of oligonucleotides with similar properties are selected, which at each stage are the most abundant. Members of these families may have specificity for the target, but they have low affinity. There are many reasons for this: the properties of either the library or the target itself, the selection procedure, etc. The selected oligonucleotides, members of the family, are not aptamers according to the classical definition. Nevertheless, the structure of such oligonucleotides (or a method for their selection) is of undoubted value, since they can be used as blanks for creation of high-affinity aptamers (or for selection procedure design) for a given target. For these oligonucleotides the term "pseudo-aptamers" could be coined; the first part of the compound word "pseudo" comes from the Greek "pseudes" in the meaning of "behaves like an aptamer, but is not an aptamer."

Nominations for INSOAP committee

We are currently asking for expressions of interest for membership of the management committee of INSOAP. If you would like to be an integral part of our Society as it moves forward, please contact me at sarah.shigdar@deakin.edu.au.

Updates to the website

We have been working on updating the website for INSOAP and you will now see that we have a listing of all aptamer companies throughout the world, as well as a listing of all the aptamer laboratories to date. If we haven't got you listed, please get in touch and we will add you to our growing list. We are also providing a careers page so please get in touch with any vacancies you wish to be listed. Finally, if there are any suggestions for improvements to the website, please contact us and we will make the changes.

Interview with a researcher: Dr Shalen Kumar

Dr Kumar started researching aptamer technology during his undergraduate studies at Victoria University of Wellington when he became passionate about providing high-quality, accurate, robust and sensitive medical diagnostic solutions for third world communities and environmental monitoring. He is the founding inventor of Auramer Bio and SELEX expert. AuramerBio focuses on developing aptamers (synthetic bio-receptors) to enable new high-end precision diagnostic solutions that are affordable and mobile. With over 10 years' experience in the development of aptamers and integration in various sensing platforms, Dr Kumar heads the team and the technical development of products and partnership management.

Q1) How did you become interested in the field of aptamers?

I was looking for an alternative way to making a pregnancy test for buffalos (there is an article about this in Nature Careers). I remembered that in one of my lectures, the lecturer from China mentioned aptamers to be alternatives. When I researched, the problem was that there were very few small molecule aptamers or well-defined methods to make aptamers for small molecules in 2007.

Q2) From your point of view, what is unique about aptamers?

Adaptability. When one really understands aptamers, there are many ways that you can manipulate the aptamers to get the application you want. Aptamers can be an intricate part of any system.

Q3) What do you think is the future of aptamers?

When I first heard of aptamers, every bit of hype was that "aptamers are antibody alternatives". I believe that the future of aptamers is really in acknowledging them as a chemical entity of their own and not based them off antibody platforms.

Q4) What are the major challenges that need to be solved?

Undertaking more fundamental science around SELEX, aptamer characterization methods, and novel applications. All this can be achieved if we collaborate together (pure researchers and commercial teams). However, facilitating this community is a challenge that we need to overcome.

Q5) Tell us about your business.

Auramer Bio was founded as a result of IP generated from my graduate research and PhD. We have 3 parts of our business:
Firstly, we started generating DNA aptamers as a fee for service mostly specializing in tricky small molecules and moved to peptides, proteins, bacterial and mammalian cells.
Second, we are developing aptamer based biosensing platform for drugs of abuse, female health, and environmental contaminants.
Third, we are providing aptamers to partnered companies who are working to develop their own platform.
We have grown in expertise and as a team over the last 5 years. We now have people who are dedicated aptamer biologists, electrochemists, assay developers, microfluidics etc.

Q6) How did you find out about the INSOAP?

I have been part of INSOAP for a while. I found out when I was a student looking for other aptamer scientist.

Q7) How do you support INSOAP?

I haven't yet but aspire to help with mentoring other young upcoming scientists and perhaps sponsoring poster prizes at conferences.

Q8) What kind of advice can you give to the young researchers about aptamers?

Be proactive and talk to as many people who are in the field of aptamers or may even be biosensor scientists. All you need to do is to learn from other experience and see how you can adapt their platforms to what you are doing with your aptamers. Collaboration is key to success.

Q9) What is your personal philosophy on life and science?

I live and love this quote "I am the only boundary to the fruition of my dreams" In life, one needs to show compassion to everyone, be honest, see everyone as equal, share knowledge, and accept any situation as a lesson. Take all this and apply, and you will always be successful at whatever you do. Science has the same philosophy, many experiments will probably not work out, rather than getting frustrated and giving up, understand and observe all the intricate parts of that experiment (ones that worked and didn't work), seek for advice from peers with experience, and take note of all before systematically repeating it sensibly.

Q10) What was your favorite part about research?

Not knowing whether something will work out the way you hope it will be. The excitement of strategically planning and designing research questions, then getting in the lab and trying is what research is about.

Q11) What do you like to do in your free time?

I have many things I do. I like a busy lifestyle. I have a lifestyle farm where I always have work to do. Spending time cutting trees for firewood, clearing shrub from gardens, fence fixing, taking care of animals are some of my chores. One of my rams acts like a dog as I raised him by bottle feeding. Then I have a very big extended family who I spend a lot of time with as well. Teaching nieces and nephews about our traditional Fijian ways of farming. Some community work is very important. When doing these things, I get the best ideas and inspirations for my work.

Q12) Any other fun facts/tidbits you'd like us to know!

I grew up with racing horses, like working on project cars, used to compete in mixed martial arts, and write philosophy on things that catch my attention.

Aptamers Journal

The Aptamers journal is the official journal of the International Society on Aptamers and will publish studies on all aspects of aptamer research. The Aptamers journal, launched at the end of 2017, is the first-ever peer-reviewed journal aimed to publishing all aspects of aptamer research. The journal is specifically open-access to help make aptamer research accessible to scientists all over the world. Moreover, the journal will consider "negative" data, as we all know that this can be very valuable information when performing aptamer research.

The landscape of published articles in the Aptamers journal to-date is very diverse. For example, topics of the presentations include selection methods, aptamer characterization, chemical modification of aptamers, applications in drug delivery and biomaterials. Furthermore, the publications have been received by authors from all over the world: specifically, USA, Germany, Russia, Australia, Canada, South Korea, Switzerland, Uruguay, Japan, Italy, China, Spain, UK, and Jordan. Finally, the journal accepts several forms of publications, and indeed each of the publication formats have included. In particular, we received three full Research Articles, three Research Reports, five Reviews/Mini-Reviews, one Protocol/Method, and three Meeting Reports/News Articles.

We would like to thank our very diverse and international Editorial Council team and reviewers for helping make the publications of these 17 or so articles a reality. We look forward to many more aptamer articles in 2020 and beyond! Please submit your articles for peer-review to the Aptamers journal. So if you'd like to publish your work in the first Aptamers journal, please follow this link http://www.JAptamers.co.uk .

Aptamer Consortium – Sarah Shigdar

One of issues that we've watched develop over the last few years is the reproducibility crisis that we first discussed in the June 2017 newsletter. At the time we suggested that aptamers could fix some of the issues of reproducibility by providing a more reliable tool for applications. The next step in this process is to develop best practice guidelines for the publication of research articles describing the generation of aptamers and their use in specific applications. To that end, within the Society, we have been discussing the need for a small group of researchers to come together from both Academia and Industry to work on these guidelines. Our Mission Statement, while still a work in progress, states:

'The Aptamer Consortium supports researchers, academic institutions, and partners, to promote best practice for aptamer techniques in both diagnostics and therapeutics, to provide guidance for basic and applied research as well as development and commercialisation, and facilitate discussion and interchange of ideas.'

We are currently working on our first paper from the Consortium, which will tackle the minimum standards for publishing novel aptamers and we hope to have that published soon. If you are interested in sharing your views on the Consortium, please email me (sarah.shigdar@deakin.edu.au).

Aptamers 2020 online

Regrettably, we had to cancel our Aptamers 2020 meeting in April due to the COVID19 pandemic. We provisionally scheduled a later version of this meeting on originally 16th and 17th September 2020. However, due to the ongoing circumstances, and considering that air travel may still not be possible by September, we are keeping our options open. If the outbreak is not under control in the next few months, we will hold an online version of this meeting on 3rd and 4th September 2020 (instead of 16th and 17th September 2020).

As a lot of our colleagues come from around the globe to attend this meeting, finding a time suitable for everyone will be difficult. Therefore, to accommodate the various time zones, the meeting be held over two days, for Asia/Australasia on day 1 and for Europe/Americas on day 2. Each day will consist of approximately three hours of talks, including 2-3 keynotes by senior researchers, and short research talks by junior researchers and students.

There will also be the opportunity to present posters.

If you would like to attend, please register your interest on the following link:

http://libpubmedia.co.uk/aptamers-2020/aptamers-2020-online

There is no alternative to face-to-face meetings, and so we hope very much to be back for our next annual congregation at Oxford in March/April 2021.