International Society on Aptamers

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EDITORIAL

Welcome to the 2019 first issue of INSOAP times, your source to what's happening in the aptamer world presented by the INSOAP team. Happy New Year everyone. I hope you had a great start to 2019. What started off as a very quiet January quickly ramped up to a very busy February and March. I am looking forward to attending our upcoming conference in Oxford as it also gives me a small break from work. I love coming back to the UK each year to catch up with colleagues at the conference and as you'll see from the upcoming report on page 2, we have some familiar faces, but we also have a lot of new names too. It promises to be another great conference. I'm also hoping that the weather last year was a bit of an anomaly and it will be a bit warmer this year. I'm also excited to announce a new initiative of INSOAP, a **consortium of researchers** that will develop best practice guidelines for aptamer publications. More of that on page 3. We are continuing to keep track of new aptamers being developed, and you'll see our new list on page 3, thanks to Maureen McKeague. And keeping with our interview series, we are excited to have Nebojsa Janjic share his thoughts.

For those of you joining us at the conference this year, I wish you safe travels. Turn to the next page for an overview of what we've got on the program this year. If you're not able to attend, follow us on Twitter (#AptaOx19), and read our conference report in the *Aptamers* Journal (http://www.JAptamers.co.uk) later in the year.

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 (@AptamerSociety, @JAptamers).

May you all have a great few months, and we'll see you in Oxford in April!

Dr Sarah Shigdar
President

Inside this issue:

Newsletter Contributors:

Dr Sarah Shigdar
Dr Maureen McKeague
Dr Muhammad Sohail

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http://aptamersociety.org
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https://twitter.com/aptamer_connect.

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. To submit an article please see: http://japtamers.co.uk/submit-a-manuscript/

Aptamers 2019 Symposium

Web: http://libpubmedia.co.uk/aptamers-2019
Twitter: @AptamerSociety; @JAptamers; #AptaOx19
Email: AptamersOxford@gmail.com

We would like to thank our Symposium Chair, Günter Mayer, for helping us put together a fantastic program for this year. In keeping with previous years, we have sub-divided the program into Therapeutics and Diagnostics, Biosensors and Probes, Riboswitches, and Chemistry, selection, technologies and innovation. We also have our flash talks session, which proved very popular last year. We have managed to secure funding for poster and flash talk prizes again and we are excited to see the quality of the research being presented from our next generation of aptamer researchers. We have a great representation of researchers from around the world, with presenters from Australia, Belgium, Canada, China, Cyprus, France, Germany, India, Italy, Japan, Qatar, Russia, South Africa, Spain, Switzerland, Turkey, UK, Uruguay, and USA.

As well as the scientific program, we will also be holding our Annual General Meeting and a discussion on the Consortium before breaking for the conference dinner. We would like to thank our sponsors (so far) for their generous support, making this meeting possible.

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Aptamers Journal

Aptamers The Official INSOAP 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. Already, we have received 15 articles; four in 2017 at the end of the year and 11 last year (2018) – that's an average of almost one per month! Our next goal is to be cited by PubMed: to qualify for the PMC application.

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 15 articles a reality. We look forward to many more aptamer articles in 2019! Please submit your articles for peer-review to the

Aptamers journal. All symposium delegates can submit an article before 30th September 2019 for free. 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 will be having a discussion about the role of the Consortium at the upcoming Symposium. If you are interested in sharing your views on the Consortium, please email me before the end of May 2019 (sarah.shigdar@deakin.edu.au).

INSOAP updated list of recently published aptamers

Maureen McKeague

Here are newly reported aptamers since our last issue (December 2018). As in our previous issues, we only report aptamers that have been characterized with a dissociation constant (Table 1). Specially, we make use of Pubmed to identify newly published aptamers with the keywords "aptamer" and "SELEX". In the last few months over 70 publications reporting new DNA, RNA, or modified nucleic acid-based aptamer sequences were published! 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 (Dec 2018).

Link	Target	Nucleic acid type
https://www.ncbi.nlm.nih.gov/pubmed/29361056	diethylthiatricarbocyanine	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29346617	ciprofloxacin	RNA
https://www.ncbi.nlm.nih.gov/pubmed/29501140	florfenicol	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29495282	Protein A	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29496467	Staphylococcal enterotoxin A	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29501140	florfenicol	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29499933	skeletal muscle-specific RNA aptamer	RNA
https://www.ncbi.nlm.nih.gov/pubmed/29499932	CI-H460 non-small-cell lung cancer cells	2'-F RNA
https://www.ncbi.nlm.nih.gov/pubmed/29505267	malachite green	RNA
https://www.ncbi.nlm.nih.gov/pubmed/29594592	Mycobacterium tuberculosis Ag85A (FbpA)	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29608400	endothelial cell lines mouse (bEND3), human (hCMEC/D3) (internalization)	RNA
https://www.ncbi.nlm.nih.gov/pubmed/29609164	H1N1 viruses	DNA

https://www.ncbi.nlm.nih.gov/pubmed/29655714	Norovirus	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29666232	prostate cancer cells	RNA
https://www.ncbi.nlm.nih.gov/pubmed/29667819	HIV reverse transcriptase	TNA
https://www.ncbi.nlm.nih.gov/pubmed/29670956	amyloid-β peptide	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29698672	Streptococcus pyogenes	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29708252	Glioblastoma multiforme cells	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29722521	Plasmodium falciparum glutamate dehydrogenase	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29724225	P. falciparum lactate dehydrogenase	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29733244	chemokine (C-C motif) ligand 21	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29756774	E. coli O157:H7	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29790932	zona pellucida	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29858057	alpha-synuclein	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29858077	mutant huntingtin	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29872833	Cefquinome	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29893086	cervical intraepithelial neoplasia	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29910175	TLR4 (toll like receptor)	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29906496	Annexin A2	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29928472	CD19	DNA
https://www.ncbi.nlm.nih.gov/pubmed/29931157	sulforhodamine B and other dyes	RNA
https://www.ncbi.nlm.nih.gov/pubmed/29964028	Streptococcus pneumonia	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30070419	gluten	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30085205	Ochratoxin A	TNA
https://www.ncbi.nlm.nih.gov/pubmed/30098503	Metastatic Breast Cancer	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30141409	Renal Cell Carcinoma	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30153406	saxitoxin, domoic acid, and tetrodotoxin	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30155822	FokI nuclease domain	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30185972	Anti-Coagulant Dabigatran Etexilate	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30205966	Tuberculous meningitis	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30216975	clenbuterol	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30251354	nonylphenol ethoxylate	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30270541	Vibrio vulnificus	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30303958	gastrointestinal cancer biomarkers CEA, CA50 and CA72-4	RNA
https://www.ncbi.nlm.nih.gov/pubmed/30336124	anaphylatoxin C5a	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30346760	zearalenone	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30368278	Lactoferrin	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30407110	CD24	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30411046	heparosan and chondroitin	RNA
https://www.ncbi.nlm.nih.gov/pubmed/30411044	atrazine	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30419633	Mixed lineage leukemia proteins	RNA
https://www.ncbi.nlm.nih.gov/pubmed/30513671	Furaneol	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30519686	CD33 positive leukemia cells	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30519686	streptavidin	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30594072	breast cancer cell lines	hydrophobic unnatural base
https://www.ncbi.nlm.nih.gov/pubmed/30594071	platelet-derived growth factor receptor α (PDGFRα)	RNA
https://www.ncbi.nlm.nih.gov/pubmed/30602113	N-methyl mesoporphyrin IX (NMM)	DNA

https://www.ncbi.nlm.nih.gov/pubmed/30609555	paclitaxel-resistant ovarian cancer cell line (A2780T)	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30609550	CD70 and SKOV-3 ovarian cells	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30609553	dickkopf-1(DKK1) (biomarker of hepatocellular carcinoma)	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30613143	bone marrow endothelial cell	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30642129	Amyloid Beta Peptide	RNA
https://www.ncbi.nlm.nih.gov/pubmed/30648555	EpCAM cells	RNA
https://www.ncbi.nlm.nih.gov/pubmed/30659315	cervical cancer Ca Ski and HeLa	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30685034	Vibrio parahaemolyticus	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30698517	rachinotus ovatus NNV (GTONNV)-infected cells	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30742800	glycated hemoglobins	2'-F RNA
https://www.ncbi.nlm.nih.gov/pubmed/30740973	Ebola virus	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30779315	Candida albicans	RNA
https://www.ncbi.nlm.nih.gov/pubmed/30779754	C4-HSL (from Pseudomonas aeruginosa)	DNA
https://www.ncbi.nlm.nih.gov/pubmed/30773785	DFHBI-1T	RNA
https://www.ncbi.nlm.nih.gov/pubmed/30794054	HP1/Swi6	RNA

Aptamers versus antibodies for cancer therapy

Sarah Shigdar

It seems to be one of the main themes of my articles for the newsletter – antibodies versus aptamers. As more and more clinical trial results are being presented for immunohterapy using antibodies, I do wonder how many more antibody based drugs are going to be developed and how much money will be spent on an area of research that so far has provided limited success. Immunotherpy works by binding to receptors on the cell surface and utilising the immune system to kill the cancer cells. Overall, this theory has merit and builds on initial research from more than 100 years ago. So why doesn't it work? There are a number of reasons for why three has been such poor results. One reason is that cancer cell have evolved to hide from the immune cells which would typically discover and attack these cells. As well, there are only a small number of cancer patients who have tumour infiltrating lymphocytes – the cells of the immune system needed to kill the cancer cells. This is typically around 15-30% of patients and was presnted at a conference I attended a few years ago (Lorne Cancer Conference, Australia). So, we knew that only about a third of patients may benefit from immunotherapy. A further update on this was presented by a member of Fiona Simpson's group in 2018 – that cancer cells are inherently hungry and when antibodies bind to the cancer cell surface, they are endocytosed in about 50% of patients. This reduces the number of patients able to be treated down to around 7.5-15%, which is what we are seeing in the majority of patients being treated, a response rate of around 10-12%. It's possible to add in drugs that block endocytosis, but this then adds to side effects experienced by the patient during treatment. We are also seeing patients that have survived immunotherapy experiencing long term issues as the antibodies ramped up the immune system with no way of turning it off and so there is a rise in autoimmune diseases. So how do we tackle this issue? We know that targeting cell surface receptors is a well recognised method of providing directed therapies. Combining this with a the rapid endocytosis seen with cancer cells and delivering drugs into the cancer cells has been tested using both antibodies and aptamers. So which is better? Antibodies have been developed for targeted drug therapy for 40 years. Antibody drug conjugates have been generated though the addition of any compound to the antibody, dur to the chemistries involved can denature the protein. Also, because of their size, they have problems getting into the tumour, which means they can't target all the cells. They can be effective in liquid cancers, as can immunotherapy, but once you get to the dynamic environment of a solid

tumour, they lose effectiveness. Aptamers work on the same basis as antibodies, but they are much smaller meaning they can overcome some of the issues of penetrating a solid tumour. The cojungation chemistries also have much less of an effect on the aptamer and are unlikely to denature its structurre. There are still some issues to resolve with aptamers, such as being prone to nuclease degradation or being removed by the reticulo-endothelial system, but results from a number of pre-clinical trials are increasingly promising. There also haven't been many reports of side effects relating to the use of aptamers, which also promises to give patients a much better quality of life during and after treatment. I'm hoping that we will start seeing more aptamers progressing to clinical trials in the next year or so to give patients a better experience during and after treatment.

Interview with a researcher: Dr Nebojsa Janjic

Dr Janjic received his bachelor's degree in molecular biology and PhD in physical organic chemistry from the University of Washington in Seattle before moving to Scripps Research Institute in L Jolla as a c Cancer Research Institute Fellow for his postdoctoral training. Prior to joining Somalogic as Chief Scientific Officer in January 2009, Nebojsa was the CSO at Replidyne Inc. and Senior Director of Drud Discovery at NeXstar Pharmaceuticals. In this latter position, he was responsible for creating a pipeline of aptamer-based drug candidates for pre-clinical and clinical development. His contributions included the discovery and early development of Macugen, the first-in-class, FDA-approved treatment for macular degeneration and Innovative Pharmaceutical Product of the Year in 2005. Dr. Janjic is also an inventor of Fovista™, an aptamer-based antagonist of PDGF-B currently in late-stage clinical trials for use in combination with VEGF inhibitors in macular degeneration.

Q1) How did you become interested in the field of aptamers?
It was kind of an accident. I read the first aptamer paper by Tuerk and Gold in Science in 1990 as a post-doc at Scripps, and although I thought it was interesting, it was pretty far outside of my field (I was working with catalytic antibodies at the time), so I did not give it much thought. Then I got a call out of the blue from Gerald (Jerry) Joyce, then at Scripps, in the summer of the following year, who asked me if I wanted to meet with Larry Gold, who, according to Jerry, was coming to give a seminar on SELEX and wanted to meet with me. My recollection is that I was quite abrupt during the first part of the call, since I had to stop my experiments to take the call on the one telephone we shared outside the lab, and since I didn't know who either Jerry or Larry were. Then, as Jerry, in his typical polite way, started to describe who Larry was, I started to recall that I had applied for a position with a company in Boulder that was based on the Science paper. As my memory cleared, my demeanor with Jerry changed dramatically, and I thanked him for the invitation to meet Larry, which I graciously accepted. This almost accidental meeting led to a visit in Boulder and a job with the first aptamer company a few months later. Serendipity can be a wonderful thing, and we can only appreciate in hindsight the importance of some events that at the time they were occurring seemed unremarkable in every way.

Q2) From your point of view, what is unique about aptamers?
The nucleic acid backbone has six rotational degrees of freedom compared to only two in proteins, so the conformational flexibility of single-stranded nucleic acids per monomer is considerably higher that most scientists appreciate. This, along with the enormous number of sequences that can be sampled in selections, leads to a shape repertoire from which ligands with exquisite shape complementarity can be selected. We are only beginning to fully appreciate the structural features with which aptamers recognize their targets, especially with some of the modifications we are now favoring in selections.

Q3) What do you think is the future of aptamers?
This still feels like a relatively new field, with many applications that remain to be fully exploited. This is especially true of aptamer-based therapeutics.

Q4) What are the major challenges that need to be solved?
This very much depends on the intended use of aptamers. For diagnostic uses, aptamers are now recognized as affinity reagents that are competitive with protein-based reagents, including antibodies. For therapeutics, there remains a need to find good matches between intrinsic properties of aptamers and indications for which these properties are well suited. In this context, metabolic stability and pharmacokinetics remain areas of intense focus. Much progress has been made in recent years with diversity-enhancing modifications that dramatically expand the range of protein targets for which a high-quality aptamer can be identified, and we intend to continue to pursue this line of research.

Q5) Tell us about your research/business.
SomaLogic is developing a new kind of a diagnostic test based on measurement of a huge number of proteins at the same time (now 5,000) and deriving information about the state of human health and wellness on the basis of quantitative assessment of multiple proteins, with the help of algorithms that convert those values into actionable metrics. The main idea is that from a single test, which can be taken on an ongoing basis, an individual can monitor their health in real time, since, unlike genes, changes in protein expression directly reflect physiological changes in the body.

Of course, we have not forgotten the fact that aptamers have a wide range of other applications, including therapeutics, so we are continuing to explore ways in which we can leverage these assets.

Q6) How did you find out about the INSOAP?
From Maureen McKeague, and the attendance of Aptamers Oxford conferences over the years.

Q7) How do you support INSOAP?
We have been supporting the Aptamers Oxford conferences with regular attendance and sponsorship.

Q8) What kind of advice can give to the young researchers about aptamers?
There is a large range of quality of science in the aptamer field. Some papers are great, some are quite poor. We as a field must keep striving to remain rigorous in all aspects of experimental design and execution, data analysis, and interpretation of results. For young researchers, this is still a young field in many ways, so the world of applications is wide open.

Q9) What is your personal philosophy on life and science?
We are all privileged to be scientists. Because we get to think about important problems that can be solved with our efforts, and because we get to do things that are interesting and generally reasonably compensated, we have some kind of an obligation to make a mark, to make some kind of difference in the world, with what we do.

Q10) What was your favorite part about research?
I get to work with super smart people. Some of them are also nice, as well as fun to be around. I consider this a major perk of the profession.

Q11) What do you like to do in your free time?
I do cherish the moments of downtime. I usually just read, over a wide spectrum of genres. I like to travel, and I often see travel for work as a perk. I run a little, ride my bike a little, hike a little and try to get just enough exercise to feel good, although I do feel that the best part of working out is being done (which does feel good). Having been a competitive rower through high school and college, I now feel I have the need for extreme fitness out of

my system, so I just kind of putter around without any impressive fitness goals (which in Boulder, by the way, is generally considered unconscionable).

Q12) Any other fun facts/tidbits you'd like us to know!
As a person who initiated the program that led to Macugen, I remain enormously interested in therapeutic applications of aptamers. I am looking for a way to do more of this kind of research in the field. There are quite specific opportunities that remain to be tapped, and I look forward to making additional contributions.

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.