

Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/jes

Professor William R. Cullen and arsenic chemistry

X. Chris Le

Division of Analytical and Environmental Toxicology, Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Alberta T6G 2G3, Canada

This special issue of the *Journal of Environmental Sciences* honors Professor William R. Cullen for his outstanding contributions to synthetic chemistry, environmental chemistry, microbiology, and toxicology of arsenic and its compounds. It is very fitting that the papers in this issue cover a diverse range of topics of arsenic research, including the synthesis of arsenic compounds (Cullen et al., 2016), analytical characterization and detection (Currier et al., 2016; Kalantzi et al., 2016; Khan and Francesconi, 2016; Sun et al., 2016), environmental chemistry (Chávez-Capilla et al., 2016; Tindale et al., 2016), treatment/removal of arsenic (Yan et al., 2016), human exposure to arsenic species (Thomas and Bradham, 2016), cellular transport of arsenic (Roggenbeck et al., 2016), transformation of arsenic species in the environment and in biological systems (Baker and Wallschläger, 2016; Foster and Maher, 2016; Guo et al., 2016; Nearing et al., 2016), and toxicology of arsenic species (Aborode et al., 2016; Cohen et al., 2016; Fujioka et al., 2016; Moe et al., 2016).

In the past two years, the *Journal of Environmental Sciences* has published several papers on the treatment and removal of arsenic from water (Cui et al., 2015; Du et al., 2014; Terracciano et al., 2015; Xia et al., 2014). The treatment technologies included coprecipitation, coagulation, and combinations of oxidation, coagulation, and filtration. Processes relevant to the treatment and mobility of arsenic, including oxidation, adsorption, and leaching, were discussed (Ding et al., 2015; Zhang et al., 2014; Córdoba et al., 2015). Two research articles (Hu et al., 2015; Pan et al., 2014) and a highlight (Newbigging et al., 2015) focused on arsenic in rice grain and roots, aiming to reduce arsenic content by controlling water irrigation. A review on detection of arsenic in water (Hao et al., 2015), an article on risk assessment of different arsenic species in the aquatic environment (Du et al., 2015), and two papers on arsenic and microorganisms (Armendariz et al., 2015; Xu et al., 2014) were also published. However, there has been no thematic issue dedicated to arsenic. This special issue of the journal highlights recent advances in arsenic research and complements other recently published papers.

Many of the papers in this special issue come from international groups that have collaborated with Dr. Cullen and benefited from his expertise. Professor Samuel Cohen from the University of Nebraska Medical Center wrote: "Dr. Bill Cullen is an outstanding scientist, a leader in arsenic research, and an excellent collaborator. He generously provided reagents to our lab, going to extraordinary lengths to have them synthesized in his laboratory and provided to us without charge. I have greatly enjoyed the scientific discussions we have had over the years since I first met him in 2000, with friendly banter, a font of incredible knowledge and a willingness to listen to ideas, no matter how farfetched." Dr. David Thomas from the National Health and Environmental Effects Research Laboratory of the United States Environmental Protection Agency (US EPA) echoed with his comments: "I owe a great debt to Bill. He gave us the methylated trivalent arsenicals that we used to start our work on the role of oxidation state in toxicity of arsenicals. He was unfailingly helpful to us in those early years, providing chemicals and good advice on our research. It was a great pleasure to work with him and to benefit from his knowledge. Bill's generosity is an exemplar of the collaborative spirit of science."

William R. Cullen was born in Dunedin, New Zealand, in 1933. Following a BSc (1955) and MSc (First Class Honours) (1957) from the University of Otago, he was awarded a New Zealand Universities Postgraduate Scholarship in Science to work with Professor H. J. Emeléus at Cambridge University (UK). His PhD (1959) work involved the synthesis of a new class of fluorocarbon derivatives of arsenic. He accepted a position at the University of British Columbia (UBC), Vancouver, Canada, in 1958 and rose through the ranks to Professor in 1969; on "retirement" in 1998 he continued his research work as Professor Emeritus. During this time he enjoyed a number of visiting professorships in the UK and Australia. He was appointed Adjunct Professor at the Royal Military College of Canada, Kingston, in 2000.

Dr. Cullen's early work at UBC on fluorocarbon derivatives of main group elements was recognized by the Chemical Institute

E-mail address: xc.le@ualberta.ca.

<http://dx.doi.org/10.1016/j.jes.2016.11.001>

1001-0742/© 2016 The Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences. Published by Elsevier B.V.

of Canada (CIC) with the Noranda Lecture Award for Inorganic and Physical Chemistry in 1973. Around 1970 Dr. Cullen became interested in the biological and environmental aspects of arsenic chemistry and was the driving force behind the establishment of the Bioinorganic Chemistry Group at UBC and the organization of the first International Conference on Bioinorganic Chemistry at UBC in 1976 (the 15th conference in this series returned to UBC in 2011). His early work on the biological methylation of arsenic was recognized as a *Milestone of Canadian Chemistry* (2000). His research on arsenic has expanded to arsenic speciation analysis (Aposhian et al., 2000; Feldmann et al., 1999; Fricke et al., 2007; Gong et al., 2001; Le et al., 2000), environmental fate (Lai et al., 2012; Le et al., 1994; Moriarty et al., 2014; Norum et al., 2005), bioaccessibility (Koch et al., 2007, 2011), biotransformation (Cullen et al., 1989; Li et al., 1996), arsenic binding to proteins (Chen et al., 2015; Jiang et al., 2003; Lu et al., 2004; Shen et al., 2013; Yan et al., 2009), arsenic toxicity (Andrewes et al., 2004; Lin et al., 1999; Petrick et al., 2000; Shen et al., 2009; Styblo et al., 1997; Vega et al., 2001; Zhang et al., 2015), and molecular biology (Sun et al., 2004). With his love for chemistry and insights into molecular fundamentals, he has always embraced and thrived in interdisciplinary research.

Perhaps because of his vast knowledge deeply rooted in chemical principles, Dr. Cullen never shies away from championing the chemistry of arsenic (Cullen, 2014). Professor Kevin Francesconi from the University of Graz (Austria) remarked: “Bill is a true chemist, and at every opportunity (papers, conferences) he tries to instill the need to understand the underlying chemistry in order to interpret the observed environmental data.” He always enjoys discussions of chemistry among colleagues and peers, better yet over a nice glass of wine or beer (Fig. 1).

Dr. Cullen has supervised more than 80 graduate students, postdoctoral fellows, visiting scholars, and technicians. Many of them hold academic positions, and their research ranges from arsenic (Aborode et al., 2016; Nearing et al., 2016; Moe et al., 2016) to other environmental contaminants (Miller-Schulze et al., 2016; Pan et al., 2016). Beyond his exemplary mentoring within his own research group, Dr. Cullen has always been generous in providing support to young scientists. Professor Miroslav Styblo from the University of North Carolina at Chapel Hill (USA) wrote: “Bill has played absolutely an essential role in my professional career, starting from my postdoctoral years in US EPA. He was the one who made it possible for us to carry out a series of studies that characterized acute toxicities and other adverse effects of methylated trivalent arsenicals (metabolites of inorganic arsenic) in various biological systems, which together with his work and work in other laboratories challenged the original concept of the methylation as a simple detoxification process for inorganic arsenic and provided evidence for the contribution of the methylated trivalent arsenicals to the adverse effects of inorganic arsenic exposure. Looking back, it is clear to me that all this progress in arsenic toxicology and biochemistry would not have been possible without Bill’s pioneering work on mechanisms of arsenic metabolism, and his advice and the critical arsenic standards he provided to our lab and to other teams around the world.” Professor Chris Orvig, a well-known bioinorganic chemist at UBC and elected Fellow of the Royal Society of Canada, provides the following compliment. “From the moment I set foot on the UBC campus in 1984 to start my faculty position, Bill was a valued mentor and friend. His office was two down from mine for about 20 years and I could always find a sympathetic ear and wise



Fig. 1 – Dr. Cullen enjoys friendly discussions with Dr. Jerry Schnoor (back left), Sandra Cohen (back right), Dr. Ken Reimer (front right), and Deborah Reimer (front left), after the 10th International Symposium on Persistent Toxic Substances, held in Edmonton, Alberta, Canada on August 13–17, 2013.

advice as his door was always open to me to moan, and then learn.” Professor David Chen, who contributed an article to honor Dr. Cullen (MacLennan et al., 2016), remarked: “Soon after I joined the Department of Chemistry at UBC in 1994, Bill invited me to his home, introduced me to his research group and collaborators, and served on supervisory committees of my students. I am very grateful to have Bill as a great colleague, and I hope to continue to benefit from his wise council for many years to come.”

Although his laboratory research, teaching, and office work kept him busy, Dr. Cullen has always emphasized the importance of appropriate environmental sampling and led by example through his active participation in field work. His trainees and co-workers have many good stories to share from many of the sampling field trips. Dr. Iris Koch, a former PhD student, now an Adjunct Associate Professor at the Royal Military College of Canada, tells the following story. “When we first got to Yellowknife on a beautiful balmy light-filled evening, Bill thought a walk around one of the lakes would be a good idea to revive after a long travel day, before a hard week of field work ahead. We started along a pathway beside a lovely lake and it wasn’t long before the mosquitoes found us. We ended up having to turn back after a short walk because of the ferocity of the mosquitoes but it wasn’t until the next morning that Bill realized one mosquito had ‘got him good’. One of his eyes was swollen completely shut and stayed that way for a couple of days. Nevertheless he geared up for sediment and water sampling, although he did wear a bug hat after that.” Dr. Joerg Feldmann, a former postdoctoral fellow in Bill’s group, now Professor at the University of Aberdeen (UK), tells a story that “involves a car accident after our sampling trip to the Meager Creek hot springs. This apparently destroyed Bill’s record of not having an accident for more than 30 years. I had just started as a postdoc in Bill’s lab at UBC and my work funded by the Alexander von Humboldt Foundation (Germany) was about volatilization of arsenic from hot springs and volcanic exhalations. Bill volunteered to drive me out into the woods (at least 100 km on logging roads) for sampling. My former supervisor from Germany, Dr. Alfred Hirner, was also at that time a visitor at Bill’s lab and we three headed north passing Whistler on the way. After a steaming day at Meager Creek we were almost home, when a guy, barely of legal driving age, turned into Highway 99 at the Squamish crossing and we hit with Bill’s tank (a big 4x4) the guy in the side. The car was a wreck, but Bill maintained his cool since nobody got hurt. The tow truck and transport for us to UBC was quickly organized. I was only sorry to be the reason why Bill ended his long run without a car accident. I am grateful to Bill, since my two years with him at UBC made it possible for me to obtain an academic position.”

“Bill has never really retired and his interest in field work continued into his 80’s when he provided scientific advice to the Campbell River Environment Committee that was concerned about arsenic contamination from an upstream coal mine. He advised the committee on the environmental implications of the arsenic and mobilized community members (many of them seniors) to develop a study design and communication plan as well as to collect water,

sediment and biological samples”, said Professor Ken Reimer of the Royal Military College of Canada. “I was privileged to be a part of this very worthwhile endeavour and was able to participate in some of the field work — missing the bitterly cold days when Bill sampled in rain, sleet and freezing conditions”.

Dr. Reimer has been collaborating with Dr. Cullen for about 40 years. They first met in late 1974 when Dr. Reimer joined the UBC Chemistry Department as a postdoctoral fellow with Professor Brian James. The weekly bioinorganic chemistry seminar series sparked Dr. Reimer’s interest in the chemistry of arsenic. “When I joined Royal Roads Military College in Victoria, BC, as an assistant professor, the distribution and speciation of arsenic in the marine environment was an excellent fit with the fledgling oceanography program. I became very interested in field work and was regularly awarded ship time aboard large research vessels. Bill became a regular participant in these research cruises along the beautiful British Columbia coast. These were exciting times combining excellent science, hard work as well as good food and wine. This collaborative work led to a much cited 1989 Chemical Reviews article – ‘Arsenic Speciation in the Environment’ (Cullen and Reimer, 1989) – that displayed a picture featuring us working at sea. Over the subsequent years we published over 50 papers together and I am very pleased that later this year the Royal Society for Chemistry will release our book – Arsenic is Everywhere: Cause for Concern? – in which we hope to make the intriguing chemistry of arsenic available to non-arsenic specialists and more accessible to the general public. I can only hope that this work is as well received as Bill’s 2008 book *Is Arsenic an Aphrodisiac? The Sociochemistry of an Element* (Cullen, 2008).”

Dr. Cullen’s significant contributions to the scientific community and to society go beyond the more than 400 papers that he has published in scientific journals. His expertise has been crucial to environmental decision making on the basis of sound science. For example, to help deal with



Fig. 2 – On the occasion of Dr. Cullen being elected Fellow of the Royal Society of Canada in 1993, he was presented a gift of artwork by Mr. Zhang-An Li who was visiting Vancouver. The Chinese calligraphy illustrates “outstanding contributions and achievements”.

an enormous issue of arsenic waste from a former gold mine, Drs. Cullen and Reimer participated in numerous community meetings to determine and communicate the fate of 300,000 tonnes of arsenic trioxide stored underground in Yellowknife, Northwest Territories, and provided insights into the real *versus* the perceived risks. Working with the Canadian International Development Agency (CIDA) on a program for the mitigation of arsenic in drinking water in Bangladesh, they undertook an extensive process that involved meeting with and advising government agencies, non-governmental organizations (NGOs), and villagers in Bangladesh. Throughout his career, Dr. Cullen has generously provided his time and expertise to a variety of government agencies, NGOs, industries, and ordinary citizens. On issues as diverse as controlling bark beetle infestations in forests, arsenic in mining waste, chicken feed additives and fertilizers, or arsenic in water, food, and drinks, Dr. Cullen's insightful advice has always been highly appreciated. He is a highly valued consultant and advisor to government agencies such as CIDA, US EPA, and the US Geological Survey. He was a member of the 1999 joint US EPA and National Research Council (NRC) committee (NRC, 1999) that led to a reduction in the U.S. arsenic drinking water guideline, and in 2014 he was invited again by the US EPA to participate in a new review of the health effects of arsenic.

Dr. Cullen served as a member of the CIC Board of Directors, as Chair of the CIC Environment Division, and as Chair of the Canadian Society of Chemistry Inorganic Chemistry Division. Professor Xing-Fang Li (CIC Fellow) from the University of Alberta, an executive member and past chair of the CIC Environment Division, appraises Bill for

“revitalizing the CIC Environment Division, fostering the environmental chemistry profession, and mentoring a generation of outstanding environmental chemists. With Bill's leadership, forward thinking, and dedication, the CIC Environment Division has become a vibrant and supportive community.” Dr. Cullen was elected a Fellow of the Royal Society of Canada (Academy of Science) in 1993 (Fig. 2). In acknowledgement of his continued contribution to chemistry and society, he was the recipient of the 2014 CIC Environment Division Research and Development Award and the 2015 Canadian Society for Chemistry E.W.R. Steacie Award, fitting tributes to an incredible scientist, mentor, and friend.

Despite being highly accomplished and internationally recognized, Bill always remains very modest and personable. In celebration of Bill's receiving the CIC Environment Division Research and Development Award in 2014, Drs. Bin Hu, Guibin Jiang, Iris Koch, Elaine Leslie, Xing-Fang Li, Elena Polischuk, Ken Reimer, William Shoty, Chris Simpson, Mirek Styblo, Hailin Wang, and Zhongwen Wang paid tribute to Bill at an award symposium that I organized in Vancouver (Fig. 3). I gave the final presentation and I talked about how we have learned from Bill on the various aspects of arsenic chemistry over the years of research. At the end of the session, Bill was invited to come to the podium and receive the award plaque, and was given an opportunity to make remarks. With tears running down his cheeks, Bill could not say a single word but handed me a note that he wanted me to read to the audience. Seeing his hand-writing on paper – *You taught me everything* – I could only look at him with the utmost respect and admiration.



Fig. 3 – Dr. Cullen enjoys an academic family photo, including some of his collaborators, his former students, and his students' students. The picture was taken in Vancouver after the special award symposium honoring Dr. Cullen for the 2014 CIC Environment Division Research and Development Award (sponsored by Dima). From left to right, front row: Deborah Reimer, Dr. Cullen, and Dr. Ken Reimer. Second row: Drs. Chris Le, Xing-Fang Li, Iris Koch, Chris Simpson, and Elena Polishchuk. Third row: Dr. Hailin Wang, Dr. Xiaowen Yan, Dr. Beibei Chen, Dr. Andre Schreiber, Dr. Michelle Nearing, and Xuan Sun. Back row: Dr. Zhongwen Wang, Dr. Bin Hu, Michael Reid, Aleksandra Popowich, Rebecca Paliwoda, and Qingqing Liu.

REFERENCES

- Aborode, F.A., Raab, A., Voigt, M., Costa, L.M., Krupp, E.M., Feldmann, J., 2016. The importance of glutathione and phytochelatin on the selenite and arsenate detoxification in *Arabidopsis thaliana*. *J. Environ. Sci.* 49, 150–161.
- Andrewes, P., DeMarini, D., Funasaka, K., Wallace, K., Lai, V.W.-M., Sun, H., et al., 2004. Do arsenosugars pose a risk to human health? The comparative toxicities of a trivalent and pentavalent arsenosugar. *Environ. Sci. Technol.* 38, 4140–4148.
- Aposhian, H.V., Zheng, B., Aposhian, M.M., Le, X.C., Cebrian, M.E., Cullen, W.R., et al., 2000. DMPS-arsenic challenge test: modulation of arsenic species, including monomethylarsonous acid, excreted in human urine. *Toxicol. Appl. Pharmacol.* 165, 74–83.
- Armendariz, A.L., Talano, M.A., Wevar Oller, A.L., Medina, M.I., Agostini, E., 2015. Effect of arsenic on tolerance mechanisms of two plant growth-promoting bacteria used as biological inoculants. *J. Environ. Sci.* 33, 203–210.
- Baker, J., Wallschläger, D., 2016. The role of phosphorus in the metabolism of arsenate by a freshwater green alga, *Chlorella vulgaris*. *J. Environ. Sci.* 49, 169–178.
- Chávez-Capilla, T., Maher, W., Kelly, T., Foster, S., 2016. Evaluation of the ability of arsenic species to traverse cell membranes by simple diffusion using octanol–water and liposome–water partition coefficients. *J. Environ. Sci.* 49. <http://dx.doi.org/10.1016/j.jes.2016.08.07>.
- Chen, B., Liu, Q., Popowich, A., Shen, S., Yan, X., Zhang, Q., et al., 2015. Therapeutic and analytical applications of arsenic binding to proteins. *Metallomics* 7, 39–55.
- Cohen, S.M., Chowdhury, A., Arnold, L.L., 2016. Inorganic arsenic: A non-genotoxic carcinogen. *J. Environ. Sci.* 49, 28–37.
- Córdoba, P., Castro, I., Maroto-Valer, M., Querol, X., 2015. The potential leaching and mobilization of trace elements from FGD-gypsum of a coal-fired power plant under water re-circulation conditions. *J. Environ. Sci.* 32, 72–80.
- Cui, J.L., Jing, C.Y., Che, D.S., Zhang, J.F., Duan, S.X., 2015. Groundwater arsenic removal by coagulation using ferric(III) sulfate and polyferric sulfate: a comparative and mechanistic study. *J. Environ. Sci.* 32, 42–53.
- Cullen, W.R., 2008. *Is Arsenic an Aphrodisiac? The Sociochemistry of an Element*. Royal Society of Chemistry, London, UK.
- Cullen, W.R., 2014. Chemical mechanism of arsenic biomethylation. *Chem. Res. Toxicol.* 27, 457–461.
- Cullen, W.R., Reimer, K.J., 1989. Arsenic speciation in the environment. *Chem. Rev.* 89, 713–764.
- Cullen, W.R., McBride, B.C., Manji, H., Pickett, A.W., Reglinski, J., 1989. The metabolism of methylarsine oxide and sulfide. *Appl. Organomet. Chem.* 3, 71–78.
- Cullen, W.R., Liu, Q., Lu, X., McKnight-Whitford, A., Peng, H., Popowich, A., Yan, X., Zhang, Q., Fricke, M., Sun, H., Le, X.C., 2016. Methylated and thiolated arsenic species for environmental and health research — a review on synthesis and characterization. *J. Environ. Sci.* 49, 7–27.
- Currier, J.M., Douillet, C., Drobna, Z., Styblo, M., 2016. Oxidation state specific analysis of arsenic species in tissues of wild-type and arsenic (+3 oxidation state) methyltransferase-knockout mice. *J. Environ. Sci.* 49, 104–112.
- Ding, W., Wang, Y.J., Yu, Y.T., Zhang, X.Z., Li, J.J., Wu, F., 2015. Photooxidation of arsenic(III) to arsenic(V) on the surface of kaolinite clay. *J. Environ. Sci.* 36, 29–37.
- Du, J.J., Jing, C.Y., Duan, J.M., Zhang, Y.L., Hu, S., 2014. Removal of arsenate with hydrous ferric oxide coprecipitation: effect of humic acid. *J. Environ. Sci.* 26 (2), 240–247.
- Du, M., Wei, D.B., Tan, Z.W., Lin, A.W., Du, Y.G., 2015. The potential risk assessment for different arsenic species in the aquatic environment. *J. Environ. Sci.* 27, 1–8.
- Feldmann, J., Lai, V.W.M., Cullen, W.R., Ma, M., Lu, X., Le, X.C., 1999. Sample preparation and storage can change arsenic speciation in human urine. *Clin. Chem.* 45, 1988–1997.
- Foster, S., Maher, W., 2016. Arsenobetaine and thio-arsenic species in marine macroalgae and herbivorous animals: accumulated through trophic transfer or produced in situ? *J. Environ. Sci.* 49, 131–139.
- Fricke, M., Zeller, M., Cullen, W.R., Witkowski, M., Creed, J., 2007. Dimethylthioarsinic anhydride: a standard for arsenic speciation. *Anal. Chim. Acta* 583, 78–83.
- Fujioka, M., Gi, M., Kawachi, S., Tatsumi, K., Ishii, N., Doi, K., et al., 2016. Examination of *in vivo* mutagenicity of sodium arsenite and dimethylarsinic acid in *gpt* delta rats. *J. Environ. Sci.* 49, 125–130.
- Gong, Z., Lu, X., Cullen, W.R., Le, X.C., 2001. Unstable trivalent arsenic metabolites, monomethylarsonous acid and dimethylarsinous acid. *J. Anal. At. Spectrom.* 16, 1409–1413.
- Guo, Y.Q., Xue, X.M., Yan, Y., Zhu, Y.G., Yang, G.D., Ye, J., 2016. Arsenic methylation by an arsenite S-adenosylmethionine methyltransferase from *Spirulina platensis*. *J. Environ. Sci.* 49, 162–168.
- Hao, J.M., Han, M.J., Han, S.M., Meng, X.G., Su, T.L., Wang, Q.K., 2015. SERS detection of arsenic in water: a review. *J. Environ. Sci.* 36, 152–162.
- Hu, P.J., Ouyang, Y.N., Wu, L.H., Shen, L.B., Luo, Y.M., Christie, P., 2015. Effects of water management on arsenic and cadmium speciation and accumulation in an upland rice cultivar. *J. Environ. Sci.* 27, 225–231.
- Jiang, G., Gong, Z., Li, X.-F., Cullen, W.R., Le, X.C., 2003. Interaction of trivalent arsenicals with metallothionein. *Chem. Res. Toxicol.* 16, 873–880.
- Kalantzi, I., Mylona, K., Sofoulaki, K., Tsapakis, M., Pergantis, S.A., 2016. Arsenic speciation in fish from Greek coastal areas. *J. Environ. Sci.* (in press).
- Khan, M., Francesconi, K.A., 2016. Preliminary studies on the stability of arsenolipids: Implications for sample handling and analysis. *J. Environ. Sci.* 49, 97–103.
- Koch, I., Serran, M., Sylvester, S., Lai, V.W.-M., Owen, A., et al., 2007. Bioaccessibility and excretion of arsenic in Niu Huang Jie Du Pian pills. *Toxicol. Appl. Pharmacol.* 222, 357–364.
- Koch, I., Moriarty, M., House, K., Sui, J., Cullen, W.R., Saper, R.B., et al., 2011. Bioaccessibility of lead and arsenic in traditional Indian medicines. *Sci. Total Environ.* 409, 4545–4552.
- Lai, V.W.-M., Kanaki, K., Pergantis, S.A., Cullen, W.R., Reimer, K.J., 2012. Arsenic speciation in freshwater snails and its life cycle variation. *J. Environ. Monit.* 14, 743–751.
- Le, X.C., Cullen, W.R., Reimer, K.J., 1994. Speciation of arsenic compounds in some marine organisms. *Environ. Sci. Technol.* 28, 1598–1604.
- Le, X.C., Lu, X., Ma, M., Cullen, W.R., Aposhian, V., Zheng, B., 2000. Speciation of key arsenic metabolic intermediates in human urine. *Anal. Chem.* 72, 5172–5177.
- Li, X.-F., Le, X.C., Simpson, C.D., Cullen, W.R., Reimer, K.J., 1996. Bacterial transformation of pyrene in a marine environment. *Environ. Sci. Technol.* 30, 1115–1119.
- Lin, S., Cullen, W.R., Thomas, D.J., 1999. Methylarsenicals and arsinothiols are potent inhibitors of mouse liver thioredoxin reductase. *Chem. Res. Toxicol.* 12, 924–930.
- Lu, M., Wang, H., Li, X.-F., Lu, X., Cullen, W.R., Arnold, L.L., et al., 2004. Evidence of hemoglobin binding to arsenic as a basis for the accumulation of arsenic in rat blood. *Chem. Res. Toxicol.* 17, 1733–1742.
- MacLennan, M.S., Tie, C., Kovalchik, K., Peru, K.M., Zhang, X.X., Headley, J.V., Chen, D.D.Y., 2016. Potential of capillary electrophoresis mass spectrometry for the characterization and monitoring of amine-derivatized naphthenic acids From oil sands process-affected water. *J. Environ. Sci.* 49, 203–212.

- Miller-Schulze, J.P., Paulsen, M., Kameda, T., Toriba, A., Hayakawa, K., Cassidy, B., et al., 2016. Nitro-PAH exposures of occupationally-exposed traffic workers and associated urinary 1-nitropyrene metabolite concentrations. *J. Environ. Sci.* 49, 213–221.
- Moe, B., Peng, H.Y., Lu, X.F., Chen, B.W., Chen, L.W.L., Gabos, S., et al., 2016. Comparative cytotoxicity of fourteen trivalent and pentavalent arsenic species determined using real-time cell sensing. *J. Environ. Sci.* 49, 113–124.
- Moriarty, M.M., Lai, V.W.-M., Koch, I., Cui, L.P., Combs, C., Krupp, E.M., et al., 2014. Speciation and toxicity of arsenic in mining-affected lake sediments in the Quinsam watershed, British Columbia. *Sci. Total Environ.* 466:90–99. <http://dx.doi.org/10.1016/j.scitotenv.2013.07.005>.
- Nearing, M.M., Koch, I., Reimer, K.J., 49, 2016. Uptake and transformation of arsenic during the reproductive life stage of *Agaricus bisporus* and *Agaricus campestris*. *J. Environ. Sci.* 49, 140–149.
- Newbigging, A.M., Paliwoda, R.E., Le, X.C., 2015. Rice: reducing arsenic content by controlling water irrigation. *J. Environ. Sci.* 30, 129–131.
- Norum, U., Lai, V.W.-M., Pergantis, S.A., Cullen, W.R., 2005. Arsenic compounds in the haemolymph of the Dungeness crab, *Cancer magister*, as determined by using high-performance liquid chromatography on-line with inductively coupled plasma mass spectrometry. *J. Environ. Monit.* 7, 122–126.
- NRC (National Research Council), 1999. *Arsenic in Drinking Water*. National Academy Press, Washington, DC.
- Pan, W.S., Wu, C., Xue, S.G., Hartley, W., 2014. Arsenic dynamics in the rhizosphere and its sequestration on rice roots as affected by root oxidation. *J. Environ. Sci.* 26 (4), 892–899.
- Pan, L., Sun, J.T., Wu, X.D., Wei, Z., Zhu, L.Z., 2016. Transformation of hydroxylated and methoxylated 2,2',4,4',5-brominated diphenyl ether (BDE-99) in plants. pp. 197–202.
- Petrick, J.S., Ayala-Fierro, F., Cullen, W.R., Carter, D.E., Aposhian, H.V., 2000. Monomethylarsonous acid (MMA^{III}) is more toxic than arsenite in Chang human hepatocytes. *Toxicol. Appl. Pharmacol.* 163, 203–207.
- Roggenbeck, B.A., Banerjee, M., Leslie, E.M., 2016. Cellular arsenic transport pathways in mammals. *J. Environ. Sci.* 49, 38–58.
- Shen, S., Lee, J., Cullen, W.R., Le, X.C., Weinfeld, M., 2009. Arsenite and its mono- and di-methylated trivalent metabolites enhance the formation of BPDE-DNA adducts in *Xeroderma pigmentosum* complementation group A cells. *Chem. Res. Toxicol.* 22, 382–390.
- Shen, S., Li, X.-F., Cullen, W.R., Weinfeld, M., Le, X.C., 2013. Arsenic binding to proteins. *Chem. Rev.* 113, 7769–7792.
- Stybło, M., Serves, S.V., Cullen, W.R., Thomas, D.J., 1997. Comparative inhibition of yeast glutathione reductase by arsenicals and arsenothiols. *Chem. Res. Toxicol.* 10, 27–33.
- Sun, Y., Polishchuk, E.A., Radoja, U., Cullen, W.R., 2004. Identification and quantification of arsC genes in environmental samples by using real time PCR. *J. Microbiol. Methods* 58, 335–349.
- Sun, Y., Liu, G., Cai, Y., 2016. Thiolated arsenicals in arsenic metabolism: occurrence, formation, and biological implications. *J. Environ. Sci.* 49, 59–73.
- Terracciano, A., Ge, J., Meng, X.G., 2015. A comprehensive study of treatment of arsenic in water combining oxidation, coagulation, and filtration. *J. Environ. Sci.* 36, 178–180.
- Thomas, D.J., Bradham, K., 2016. Role of complex organic arsenicals in food in aggregate exposure to arsenic. *J. Environ. Sci.* 49, 86–96.
- Tindale, K.J., Patel, P.J., Wallschläger, D., 2016. Characterization of colloidal arsenic at two abandoned gold mine sites in Nova Scotia, Canada using asymmetric field flow fractionation inductively coupled plasma mass spectrometry. *J. Environ. Sci.* 49, 189–196.
- Vega, L., Stybło, M., Patterson, R., Cullen, W., Wang, C., Germolec, D., 2001. Differential effects of trivalent and pentavalent arsenicals on cell proliferation and cytokine secretion in normal human epidermal keratinocytes. *Toxicol. Appl. Pharmacol.* 172, 225–232.
- Xia, S.Q., Shen, S., Xu, X.Y., Liang, J., Zhou, L.J., 2014. Arsenic removal from groundwater by acclimated sludge under autohydrogenotrophic conditions. *J. Environ. Sci.* 26 (2), 248–255.
- Xu, Y.Q., Yang, M., Yao, T., Xiong, H.X., 2014. Isolation, identification and arsenic-resistance of *Acidithiobacillus ferrooxidans* HX3 producing schwertmannite. *J. Environ. Sci.* 26 (7), 1463–1470.
- Yan, H., Wang, N., Weinfeld, M., Cullen, W.R., Le, X.C., 2009. Identification of arsenic-binding proteins in human cells by affinity chromatography and mass spectrometry. *Anal. Chem.* 81, 4144–4152.
- Yan, L., Hu, S., Jing, C.Y., 2016. Recent progress of arsenic adsorption on TiO₂ in the presence of coexisting ions: a review. *J. Environ. Sci.* 49, 74–85.
- Zhang, L.K., Yang, H., Tang, J.S., Qin, X.Q., Yu, A.Y., 2014. Attenuation of arsenic in a karst subterranean stream and correlation with geochemical factors: a case study at Lihu, South China. *J. Environ. Sci.* 26 (11), 2222–2230.
- Zhang, J., Koch, I., Gibson, L.A., Loughery, J.R., Martyniuk, C.J., Button, M., et al., 2015. Transcriptomic responses during early development following arsenic exposure in western clawed frogs, *Silurana tropicalis*. *Toxicol. Sci.* 148 (2), 603–617.