# Highlight: The 5th International Symposium on Kallikreins and Kallikrein-Related Peptidases

DOI 10.1515/hsz-2014-0228

The 5th International Symposium on Kallikreins and Kallikrein-Related Peptidases (ISK2013) was held in Toronto, Canada from 28 September to 1 October, 2013. Organized by Dr. George Yousef (President) and Dr. Maria Pasic (Vice President), ISK2013 took place at the Li Ka Shing Knowledge Institute of St. Michael's Hospital, under the auspices of the Department of Laboratory Medicine and Pathobiology, University of Toronto. Invited talks were delivered by international experts in all areas of kallikrein research and covered a wide spectrum of mechanistic studies and clinical applications. The symposium provided an opportunity for young scientists and trainees to present and interact with experts in the field. The goal of ISK2013 was to review basic and clinical aspects of kallikrein research and stimulate discussion and collaboration between the participants.

Over 150 delegates from 14 countries participated in ISK2013. The nine symposia covered a wide spectrum of topics including: (a) structural and functional aspects of kallikreins; (b) kallikreins as cancer biomarkers; (c) kallikreins in skin and inflammatory disorders; (d) genetic and epigenetic regulation and signaling of kallikreins; (e) the role of kallikreins in tumor initiation and progression; (f) kallikreins in prostate. The symposium was concluded with a round table discussion on the future of kallikrein research.

The symposium began with a number of awards. Dr. Georgia Sotiropoulou was awarded the Frey-Werle Promotion Prize for her work on kallikrein function by using animal models. Dr. Morley Hollenberg was awarded the Frey-Werle Commemorative Gold Medal for his work related to kallikrein signaling through proteinase-activated receptors. Dr. Ulf Meyer-Hoffert was presented with the Frey-Werle Young Investigator award for his work on the characterization of SPINK6 proteinase inhibitor in mouse skin.

The International Society for Enzymology-sponsored lecture was delivered by Dr. Daniel Chan, the President of ISE, and was entitled 'Looking for the next generation of cancer biomarkers beyond kallikreins: glycoproteomics?'

Many lecturers who presented at the ISK2013 are included in this highlight issue of Biological Chemistry. Kallikrein research is continuously expanding and it now represents an exciting field. The Diamandis laboratory provided a comprehensive review of putative kallikrein substrates and speculated on the role of kallikreins in various pathobiological functions (Yu et al., 2014). Guo and colleagues examined glycan trees as potential regulators of activation and activity of KLKs (Guo et al., 2014). The Simmer group presented the evolution of KLK4 as an extracellular matrix enzyme critical in dental enamel maturation (Kawasaki et al., 2014). The Clements group examined the link between tissue kallikrein and KLK-regulated peptidases (Dong et al., 2014). The same group performed an analysis of the androgen and anti-androgen regulation of KLK-related peptidases 2, 3 and 4 in prostate cancer (Lai et al., 2014) and found that KLK4 is a key regulator of the tumor microenvironment in prostate cancer. Darmoul and colleagues found that KLK7 is an aberrantly expressed proliferative factor in human colon cancer (Walker et al., 2014). Courty and colleagues raised monoclonal antibodies against human KLK6 and used them to develop an immunofluorescence assay for free KLK6 (Ott et al., 2014). The same group examined KLK6 regulation by activation of proteinase-activated receptor 2 and epidermal growth factor receptor (EGFR) (Michel et al., 2014). The Scorilas group analyzed mRNA expression of KLK4 in patients with laryngeal squamous cell carcinoma and found that low expression of KLK4 is a predictor of relapse in these patients (Foteinou et al., 2014). Yousef and colleagues examined the crosstalk between miRNA and kallikreins and reported a miRNA network that may be linked to the progression of prostate cancer (Samaan et al., 2014). The same group uncovered the significance of human kallikreins KLK6 and KLK10 in gastric cancer (Kolin et al., 2014). Hollenberg and colleagues shed new light into KLK actions as signaling molecules through proteinase-activated receptors (Hollenberg, 2014). Hovnanian's group examined Netherton syndrome and found that defective kallikrein inhibition in the skin can lead to inflammation and allergy (Furio and Hovnanian, 2014). Conversely, Panos and co-workers (Panos et al., 2014) found that differential expression of multiple KLKs plays a unique role in adaptive immunity by using a new model of multiple sclerosis.

In closing we are grateful to all attendees, speakers and abstract presenters at ISK2013. We would also like to thank all authors who submitted their work to this special issue of *Biological Chemistry*. We are looking forward to the next ISK meeting (ISK2015) in Australia.

# References

- Dong, Y., Harrington, B.S., Adams, M.N., Wortmann, A., Stephenson, S.A., Lisle, J., Herington, A., Hooper, J.D., and Clements, J.A. (2014). Activation of membrane bound proteins and receptor systems: a link between tissue kallikrein and the KLK-related peptidases. Biol. Chem. 395, 977–990.
- Foteinou, E., Kontos, C.K., Giotakis, A.I., and Scorilas, A. (2014). Low mRNA expression levels of kallikrein-related peptidase 4 (*KLK4*) predict short-term relapse in patients with laryngeal squamous cell carcinoma. Biol. Chem. *395*, 1051–1062.
- Furio, L. and Hovnanian, A. (2014). Netherton syndrome: defective kallikrein inhibition in the skin leads to skin inflammation and allergy. Biol. Chem. 395, 945–958.
- Guo, S., Skala, W., Magdolen, V., Brandstetter, H., and Goettig, P. (2014). Sweetened kallikrein-related peptidases (KLKs): glycan trees as potential regulators of activation and activity. Biol. Chem. 395, 959–976.
- Hollenberg, M.D. (2014). KLKs and their hormone-like signaling actions: a new life for the PSA-KLK family. Biol. Chem. *395*, 915–929.
- Kawasaki, K., Hu, J.C-C., and Simmer, J.P. (2014). Evolution of *Klk4* and enamel maturation in eutherians. Biol. Chem. 395, 1003–1013.
- Kolin, D.L., Sy, K., Rotondo, F., Bassily, M.N., Kovacs, K., Brezden-Masley, C., Streutker, C.J., and Yousef, G.M. (2014). Prognostic significance of human tissue kallikrein-related peptidases 6 and 10 in gastric cancer. Biol. Chem. 395, 1087–1093.
- Lai, J., An, J., Nelson, C.C., Lehman, M.L., Batra J., and Clements, J.A. (2014). Analysis of androgen and anti-androgen regulation of KLK-related peptidase 2, 3, and 4 alternative transcripts in prostate cancer. Biol. Chem. *395*, 1127–1132.
- Michel, N., Heuzé-Vourc'h, N., Lavergne, E., Parent, C., Jourdan, M.-L., Vallet, A., Iochmann, S., Musso, O., Reverdiau, P., and Courty, Y. (2014). Growth and survival of lung cancer cells:

regulation by kallikrein-related peptidase 6 via activation of proteinase-activated receptor 2 and the epidermal growth factor receptor. Biol. Chem. *395*, 1015–1025.

- Ott, C., Ainciburu, M., Parent, C., Michel, S., Roesch, C., Vourc'h, P., Corcia, P., Heuze-Vourc'h, N., Jolivet-Reynaud, C., and Courty, Y. (2014). Development of monoclonal antibodies to human kallikrein-related peptidase 6 (KLK6) and their use in an immunofluorometric assay for free-KLK6. Biol. Chem. 395, 1119–1126.
- Panos, M., Christophi, G.P., Rodriguez, M., and Scarisbrick, I.A. (2014). Differential expression of multiple kallikreins in a viral model of multiple sclerosis points to unique roles in the innate and adaptive immune response. Biol. Chem. 395, 1063–1073.
- Samaan, S., Lichner, Z., Ding, Q., Saleh, C., Samuel, J., Streutker C., and Yousef, G.M. (2014). Kallikreins are involved in a miRNA network that contributes to prostate cancer progression. Biol. Chem. 395, 991–1001.
- Walker, F., Nicole, P., Jallane, A., Soosaipillai, A., Mosbach, V.,
  Oikonomopoulou, K., Diamandis, E.P., Magdolen, V., and
  Darmoul, D. (2014). Kallikrein-related peptidase 7 (KLK7) is a proliferative factor that is aberrantly expressed in human colon cancer. Biol. Chem. *395*, 1075–1086.
- Yu, Y., Prassas, I., and Diamandis, E.P (2014). Putative kallikrein substrates and their (patho)biological functions. Biol. Chem. 395, 931–943.

## George M. Yousef

Department of Laboratory Medicine St. Michael's Hospital and Department of Laboratory Medicine and Pathobiology University of Toronto, Canada e-mail: yousefg@smh.ca

#### Maria Pasic

Department of Laboratory Medicine St. Joseph's Health Centre, Toronto and Department of Laboratory Medicine and Pathobiology University of Toronto, Canada e-mail: pasicm@stjoe.on.ca

### **Eleftherios P. Diamandis**

Department of Pathology and Laboratory Medicine Mount Sinai Hospital, Department of Clinical Biochemistry University Health Network and Department Laboratory Medicine and Pathobiology University of Toronto, Canada e-mail: ediamandis@mtsinai.on.ca