

13th International Workshop on Resistance to Thyroid Hormone and Thyroid Hormone Action

Graham R. Williams¹, Anita Boelen², Samuel Refetoff³

¹Molecular Endocrinology Laboratory, Department of Medicine, Imperial College London, London, UK

²Department of Endocrinology, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands

³Departments of Medicine & Pediatrics and Committee on Genetics, The University of Chicago, Chicago, IL, USA

The 13th International Workshop on Resistance to Thyroid Hormone (IWRTH) will be held on 11-14 September 2018 in Doorn, The Netherlands, immediately before the 41st Annual Meeting of the European Thyroid Association in Newcastle, United Kingdom, which commences on Saturday 15th September. The venue, Landgoed Zonheuvel, is situated in a quiet location on the main road between Maarn and Doorn in the Utrechtse Heuvelrug, a 10,000 hectare (25,000 acre) wooded National Park area covering a glacial ridge of heathlands, shifting sands, forests, grass lands and floodplains that covers part of the province of Utrecht. Travel details to this well-connected region can be found on the workshop website along with information and links regarding connections to the ETA meeting in Newcastle.

The IWRTH meeting brings together clinicians, basic scientists and senior investigators working on thyroid hormone action and the syndromes of impaired sensitivity to thyroid hormone (ISRTH). Importantly, the workshop will maintain the tradition of encouraging active participation of young investigators, who represent the future of research and who will be eligible for accommodation and travel support because of generous sponsorship from the American Thyroid Association, European Thyroid Association, UK Society for Endocrinology as well as private donations.

Thirty-nine presentations from leading international laboratories will include the latest research on the role of thyroid hormone transport, metabolism and receptors in human ISRTH syndromes and animal models. Sessions will be devoted to: thyroid hormone transporters, deiodinase and selenoprotein biology, gene defects and treatment; and RTH α and RTH β syndromes resulting from thyroid hormone receptor mutations, incorporating discussion of unusual clinical cases and therapeutic possibilities. Further topics will focus on novel mechanisms of thyroid hormone action including new receptor ligands, the role of thyroid hormones in development, aging, inflammation, tissue degeneration and repair, and in specific target tissues.

The format of the meeting will be similar to previous workshops with particular emphasis on younger investigators and scientists presenting data on behalf of their laboratories. Sessions are structured to include equal amounts of time for both presentation and debate

in order to promote extensive discussion among participants. Apart from brief optional abstracts, there will be no published proceedings, enabling groups to present their latest, unpublished observations. There will also be a new opportunity to submit abstracts containing novel data of exceptional interest for one of two late-breaking oral presentations. Shared meals, breaks, poster sessions and activities will enhance interaction. This is an important and highly-valued tradition that facilitates engagement throughout the meeting for the benefit of all attendees and especially for younger scientists and students.

Since its inception 25 years ago in 1993, the workshop has grown in stature and earned international esteem. At the first meeting in Cambridge UK, a consensus statement was issued establishing the nomenclature of thyroid hormone receptor β gene (*THRB*) mutations in classical RTH (1-5), first described in humans in 1967 (6). At the third meeting in Aspen CO USA in 1997, the first mouse models of RTH were presented and their major role in advancing understanding of the mechanism of thyroid hormone action emerged. During the seventh meeting in Lyon, France in 2005 considerable attention was paid to new details concerning the structure, molecular biology, physiology and pharmacology of the thyroid hormone receptors (7) as well as the broadening definition of thyroid hormone hyposensitivity. Indeed, by the time of the eighth workshop on the Azorean Island of San Miguel in 2007, a new term "reduced sensitivity to thyroid hormone (RSTH)" was adopted and accepted as the field advanced (8). Furthermore, following discovery of patients with RTH α due to mutations affecting the thyroid hormone receptor α gene (*THRA*) around the time of twelfth meeting in Quebec City, Canada in 2012 it became apparent that understanding of RTH should be re-classified to include possible inherited forms of impaired sensitivity to thyroid hormone that might occur at the level of thyroid hormone transport, metabolism and receptor (9-11)fl. By the most recent meeting in Colorado Springs, USA in 2016 new possible sub-types of thyroid hormone receptor defects were hypothesized (12), and new mouse models first discussed at that workshop have now transformed the field as we embark on a new and unexpected journey that may ultimately resolve the intricacies of thyroid hormone action (13).

The stage is thus set for an exciting and outstanding 13th International Workshop on Resistance to Thyroid Hormone in The Netherlands this September in which we know participation will be enthusiastic, controversial and forthright, but absolutely certain to advance the field and our understanding.

References

1. Beck-Peccoz P, Chatterjee VK, Chin WW, DeGroot LJ, Jameson JL, Nakamura H, Refetoff S, Usala SJ, Weintraub BD 1994 Nomenclature of thyroid hormone receptor beta gene mutations in resistance to thyroid hormone: consensus statement from the first workshop on thyroid hormone resistance, July 10-11th 1993, Cambridge, U.K. *Thyroid* **4**:135-137.
2. Beck-Peccoz P, Chatterjee VK, Chin WW, DeGroot LJ, Jameson JL, Nakamura H, Refetoff S, Usala SJ, Weintraub BD 1994 Nomenclature of thyroid hormone receptor beta gene mutations in resistance to thyroid hormone. First workshop on thyroid hormone resistance, July 10-11, 1993, Cambridge, U.K. *J Endocrinol Invest* **17**:283-287.
3. Beck-Peccoz P, Chatterjee VK, Chin WW, DeGroot LJ, Jameson JL, Nakamura H, Refetoff S, Usala SJ, Weintraub BD 1994 Nomenclature of thyroid hormone receptor beta-gene mutations in resistance to thyroid hormone: consensus statement from the first workshop on thyroid hormone resistance, July 10-11, 1993, Cambridge, United Kingdom. *J Clin Endocrinol Metab* **78**:990-993.
4. Beck-Peccoz P, Chatterjee VK, Chin WW, DeGroot LJ, Jameson JL, Nakamura H, Refetoff S, Usala SJ, Weintraub BD 1994 Nomenclature of thyroid hormone receptor-beta gene mutations in resistance to thyroid hormone: consensus statement from the First Workshop on Thyroid Hormone Resistance, 10-11th July 1993, Cambridge, UK. *Eur J Endocrinol* **130**:426-428.
5. Beck-Peccoz P, Chatterjee VK, Chin WW, DeGroot LJ, Jameson JL, Nakamura H, Refetoff S, Usala SJ, Weintraub BD 1994 Nomenclature of thyroid hormone receptor beta gene mutations in resistance to thyroid hormone: consensus statement from the First Workshop on Thyroid Hormone Resistance, 10-11 July 1993, Cambridge, UK. *Clin Endocrinol (Oxf)* **40**:697-700.

6. Refetoff S, DeWind LT, DeGroot LJ 1967 Familial syndrome combining deaf-mutism, stippled epiphyses, goiter and abnormally high PBI: possible target organ refractoriness to thyroid hormone. *J Clin Endocrinol Metab* **27**:279-294.
7. Flamant F, Baxter JD, Forrest D, Refetoff S, Samuels H, Scanlan TS, Vennstrom B, Samarut J 2006 International Union of Pharmacology. LIX. The pharmacology and classification of the nuclear receptor superfamily: thyroid hormone receptors. *Pharmacol Rev* **58**:705-711.
8. Refetoff S 2008 Resistance to thyroid hormone: one of several defects causing reduced sensitivity to thyroid hormone. *Nat Clin Pract Endocrinol Metab* **4**:1.
9. Refetoff S, Bassett JH, Beck-Peccoz P, Bernal J, Brent G, Chatterjee K, De Groot LJ, Dumitrescu AM, Jameson JL, Kopp PA, Murata Y, Persani L, Samarut J, Weiss RE, Williams GR, Yen PM 2014 Classification and proposed nomenclature for inherited defects of thyroid hormone action, cell transport, and metabolism. *Thyroid* **24**:407-409.
10. Refetoff S, Bassett JH, Beck-Peccoz P, Bernal J, Brent G, Chatterjee K, De Groot LJ, Dumitrescu AM, Jameson JL, Kopp PA, Murata Y, Persani L, Samarut J, Weiss RE, Williams GR, Yen PM 2014 Classification and proposed nomenclature for inherited defects of thyroid hormone action, cell transport, and metabolism. *J Clin Endocrinol Metab* **99**:768-770.
11. Refetoff S, Bassett JH, Beck-Peccoz P, Bernal J, Brent G, Chatterjee K, De Groot LJ, Dumitrescu AM, Jameson JL, Kopp PA, Murata Y, Persani L, Samarut J, Weiss RE, Williams GR, Yen PM 2014 Classification and proposed nomenclature for inherited defects of thyroid hormone action, cell transport, and metabolism. *Eur Thyroid J* **3**:7-9.
12. Flamant F, Cheng SY, Hollenberg AN, Moeller LC, Samarut J, Wondisford FE, Yen PM, Refetoff S 2017 Thyroid Hormone Signaling Pathways: Time for a More Precise Nomenclature. *Endocrinology* **158**:2052-2057.

- 13.** Hones GS, Rakov H, Logan J, Liao XH, Werbenko E, Pollard AS, Praestholm SM, Siersbaek MS, Rijntjes E, Gassen J, Latteyer S, Engels K, Strucksberg KH, Kleinbongard P, Zwanziger D, Rozman J, Gailus-Durner V, Fuchs H, Hrabe de Angelis M, Klein-Hitpass L, Kohrle J, Armstrong DL, Grontved L, Bassett JHD, Williams GR, Refetoff S, Fuhrer D, Moeller LC 2017 Noncanonical thyroid hormone signaling mediates cardiometabolic effects in vivo. *Proc Natl Acad Sci U S A* **114**:E11323-E11332.