CSEM The Canadian Society of Endocrinology and Metabolism | SCEM La Société canadienne d'endocrinologie et de métabolisme

Hypoparathyroidism 2025 Summit:
Translating Science from the Laboratory to the Clinic
July 11, 2025
Yerba Buena Salon 8 room, San Francisco Marriott Marquis
780 Mission St, San Francisco, USA

Faculty

- Summit Chairs: Maria Luisa Brandi, Aliya A. Khan
- Scientific Planning Committee: Wenhan Chang, Michael T. Collins, Arthur Conigrave, Noriko Makita, Thomas J. Gardella, Kelly Rosko

Learning Objectives

At the end of the 2025 Parathyroid Summit, participants will be able to:

- Identify unmet needs in the diagnosis and medical management of hypoparathyroidism
- Outline recent insights in Calcium-Sensor Receptor (CaSR) activation and the potential of calcilytics
- Discuss advances in PTH basic research and corresponding clinical implications
- Describe advances in cell therapies research and corresponding clinical implications

Agenda

0800-0815 Arrival & registration **BREAKFAST PROVIDED**

I. INTRODUCTION 0815-0830

Moderators: Maria Luisa Brandi, Aliya Khan

a. The History of the Summit and Future Projections - *Aliya Khan*
b. Why Focus on Basic Research? - *Maria Luisa Brandi*

0830-0930

II. BACKGROUND

Moderators: Dolores Shoback, John P. Bilezikian

a. Diagnosis of Hypoparathyroidism: Unmet Needs - *Michael Mannstadt*

- Differential diagnosis between hypoparathyroidism and hypocalcemia
- Learn when and how to screen for hypoparathyroidism after neck surgery. (timing, biochemical markers, and clinical indicators)
- Improve recognition of hypocalcemia symptoms and appropriate testing for hypoparathyroidism.
  (emphasis on improving physician awareness and diagnostic vigilance)
- Review next diagnostic steps once hypocalcemia and low PTH are confirmed (additional biochemical blood and urine testing, genetic testing when appropriate)

b. Medical Management of Hypoparathyroidism: Unmet Needs - *Aliya Khan*

- Understand limitations of current therapy for both conventional and PTH replacement
- Know how to evaluate and monitor long term complications
- Recognize advances in research which may address unmet needs

c. Quality of Life: Unmet Needs – Heide *Siggelkow*

- Understand what is meant with Quality of Life (QoL) and how it can be measured inpatient with hypoparathyroidism
- Learn how QoL is reduced in hypoparathyroidism compared to normative controls and to disease specific controls
- Understand what influences QoL I patients with hypoparathyroidism and how it can be improved

Panel Q&A

0930-1100
III. CaSR AS A TARGET
Moderators: Michael Collins, Steven Ing

a. Development of Calcilytics - *Ed Nemeth*

- Describe how negative allosteric modulators of the CaR
- decrease the sensitivity to extracellular calcium
- increase the secretion of PTH and renal reabsorption of calcium
- normalize blood calcium levels in animal models of ADH1, ADH2, and post-surgical hypoparathyroidism

b. Promiscuous G protein activation by the CaSR - *Hao Zuo*
Structural Insights into Calcium-Sensing Receptor (CaSR):

- Describe the activation mechanisms of CaSR by calcium and amino acids.
- Differentiate among the G protein coupling selectivity of CaSR
- Identify the allosteric modulator binding sites on CaSR

c. **Activating CaSR Variant with Biased Signaling and Proposed Role in Galpha11 activation** – *Caroline Gorvin*

- Describe the similarities and differences in how individuals present with autosomal dominant hypocalcemia type-1 and type-2.
- Explain how mutations in CaSR may contribute to biased signaling.
- Identify how genetic mutations in the CaSR and Gα11 may contribute to growth.

d. Update on Encaleret in ADH1 and Postsurgical Hypoparathyroidism - *Kelly Roszko*

- Review the action of negative modulation of the CaSR at the parathyroid and kidney
- Summarize the data surrounding the use of Encaleret in ADH1
- Discuss the rationale for using a CaSR negative allosteric modulator to treat patients with postsurgical hypoparathyroidism.
- Present preliminary findings for the use of Encaleret in postsurgical hypoparathyroidism

e. **Regulation of Tonic PTH Secretion by b-Amyloid Signaling - *Wenhan Chang***
   - Mechanism controlling tonic PTH secretion
   - dimerization of CaSR with GABAbR1 mediates tonic PTH secretion.
   - b-amyloid serves as an endogenous agonist of the CaSR/GABAbR1 heterodimer
   - Vitamin D deficiency promotes b-amyloidogenesis to promote tonic PTH secretion in primary hyperparathyroidism

Panel Q&A (15 min)

1100-11:20 BREAK

1120-1300
IV. PTH PEPTIDES
Moderators: Mishaela Rubin, Jad Sfeir

a. **PTH1-34 - *Karen Winer***
   - Describe the pharmacodynamic responses to PTH 1-34 and discuss how they vary according to the different disease etiologies
   - Discuss the impact of the magnitude of PTH doses on therapeutic outcomes
   - Compare delivery methods of PTH including subcutaneous injection, pump, and oral considering multiple factors including their ability to normalize serum, urine minerals and markers of bone turnover

b. **PTH1-84 - *Bart Clarke***
   - Describe the physiology of PTH 1-84
   - Appreciate the clinical application of PTH 1-84 in treating chronic hypoparathyroidism
   - Summarize issues leading to discontinuation of rhPTH 1-84
   - Review what was learned from rhPTH 1-84

c. **Palopegteriparatide**
   Basic Research – *Kennett Sprogøe*
   - Understand the fundamentals of Transient Conjugation (TransCon) prodrug Technology
   - (Incl. how modification of various prodrug components support different therapeutic objectives)
   - Understand how Patient Centric Drug Design has been applied in the design of palopegteriparatide
   - Update: latest evidence of efficacy (what is the post-marketing

Clinical Development– *Aliya Khan (15min)*

- Understand structure of the phase 2 and phase 3 trials
- Know the impact of palopegteriparatide both RCT and LTE on patient important and surrogate outcomes
- Know how to implement and monitor therapy
- Recognize knowledge gaps and plans to address these gaps

Once weekly Canvuparatide – Richard DiMarchi

- Basic Research
- Clinical Development

Panel Q&A (10 min)

1300-1400 LUNCH PROVIDED

1400-1445
V. PTH1R AS A TARGET
Moderators: Michael Levine, Ghada El Haj Fuleihan

a. **Eneboparatide**

Basic Research - *Thomas Gardella*

- Describe the medical need for a long-acting PTH analog for the treatment of hypoparathyroidism.
- Discuss how eneboparatide emerged from basic studies on the modes of binding and signaling used by the endogenous ligands, PTH and PTHrP, at the PTH1R target receptor.
- Describe how eneboparatide uses a unique mode action involving stable binding and prolonged signaling at the PTH1R, likely from internalized cellular compartments.
- Identify differences in the modes of action used by eneboparatide and other PTH-based therapies in use or emerging for hypoparathyroidism and designed to have prolonged pharmacokinetics.

Clinical Development - *Maria Luisa Brandi*

- Discuss the clinical development of Eneboparatide
- Summarize phase 1 studies, phase 2 and 3 clinical studies

Panel Q&A (15 min)

1445-1515
VI. CELL THERAPIES & PARATHYROID TRANSPLANT
Moderators : Arthur Conigrave, Noriko Makita

a. **Parathyroid Transplant: Past, Present & Future – *Michael Levine (15 min)***

b. **Cell Therapy in Hypoparathyroidism – *Diane Krause 15 min***

- Learn how pluripotent stem cell therapy compares with parathyroid transplantation
  Be able to identify examples of successful pluripotent stem cell derived cell therapy
  Provide up to date summary of research on derivation of parathyroid cells from pluripotent stem cells
- Determine the feasibility of cell therapy for Hypopara based on overcoming the current scientific and financial challenges.

Panel Q&A 15 min

1515-1600
VII. PANEL DISCUSSION: Physician and patient expectations for new drugs in market or upcoming
Patty Keating and Michele Rayes, Patient Advocates