

bone structure and strength, supporting findings from the aforementioned *ENPP1* polymorphism study describing increased SPW in the NN and FS regions. This work contributes to the nascent body of literature studying the impact of *ENPP1* on skeletal homeostasis.

## Bone and Mineral Metabolism

### PARATHYROID AND RARE BONE DISORDERS

#### *Hypophosphatemia Gene Panel Sponsored*

#### *Program: A High Yield of Molecular Diagnoses from Clinically Confirmed XLH and Suspected Genetic Hypophosphatemia*

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X-linked hypophosphatemia (XLH), a dominant disorder caused by a disease-associated variant in the *PHEX* gene, affects males and females of all ages. Rickets and osteomalacia may be present along with short stature, lower limb deformity, muscle pain and/or weakness/fatigue, bone pain, joint pain/stiffness, hearing difficulty, enthesopathy, osteoarthritis, and dental abscesses. Patients with XLH have below-normal serum phosphate and elevated serum FGF23. XLH is one of multiple etiologies of hypophosphatemia; depending on genetic cause, management may differ. Acquired hypophosphatemia (e.g. tumor induced osteomalacia) is non-hereditary in nature. This program provides a no-charge genetic test to confirm a clinical XLH diagnosis or to aid suspected genetic hypophosphatemia diagnosis. Patients aged  $\geq 6$  months with either a clinical XLH diagnosis or suspicion of genetic hypophosphatemia, as evidenced by 2 or more clinical signs/symptoms, were eligible for testing. The next generation sequencing panel includes 13 genes: *ALPL*, *CLCN5*, *CYP2R1*, *CYP27B1*, *DMP1*, *ENPP1*, *FAH*, *FAM20C*, *FGF23*, *FGFR1*, *PHEX*, *SLC34A3* and *VDR*. Copy number variant detection was performed. 831 unrelated individuals were tested as of June 30, 2020. 569 (68.5%) of these subjects had a *PHEX* variant: 519 (91.2%) were either pathogenic or likely pathogenic (P/LP) and 50 (8.8%) were variants of uncertain significance (VUS). Of the 312 (37.5%) cases where no *PHEX* molecular diagnosis was found, 38 (12.2%) had molecular diagnoses associated with other genes/disorders: 4 had a variant (P/LP) in *FGF23* (autosomal dominant [AD] hypophosphatemic rickets), 2 had two variants (P/LP) in *CYP27B1* (autosomal recessive [AR] vitamin D dependent rickets), 1 had P/LP variants in *ENPP1* (AR hypophosphatemic rickets Type 2). There were 27 cases with single P or LP variants in *ALPL* (AD hypophosphatasia, HPP); 4 cases carried two variants (P/LP) in *ALPL* (AR form). Of 237 unique P/LP *PHEX* variants detected: 59 were deletions, duplications or insertions; 37 were copy number variants; 52 were splice-site variants; 89 were single nucleotide variants. Additional family member testing/clinical information resulted in 48

cases having VUS reclassified to P/LP, highlighting the value of cascade family testing/clinical info to resolve VUS. RNA analyses to resolve VUS may further improve molecular diagnostic yield. Program results demonstrate a high diagnostic yield for XLH/ genetic hypophosphatemia and new insight into XLH-associated *PHEX* variants.

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### PARATHYROID AND RARE BONE DISORDERS

#### *Improving Knowledge of MRONJ Risk Among Singapore Dental Practitioners Using an Educational Lecture With an Incorporated Quiz*

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**Background:** Fear of rare medication side effects, such as medication related osteonecrosis of the jaw (MRONJ) in patients and dentists remains a major reason for the low rate of antiresorptive initiation for osteoporosis, and for the poor adherence after starting treatment. In this study, we assessed the understanding of osteoporosis treatment and its risk in dental professionals pre and post an education lecture. **Method:** Dental professionals were invited to an educational lecture on osteoporosis treatment and benefits. 2 lectures were conducted over the course of a year, with the 2<sup>nd</sup> lecture conducted virtually due to physical meeting restrictions in place for the COVID 19 pandemic. Attendees were invited to submit responses to a pre- and post- lecture survey assessing their knowledge of the current osteoporosis treatments and MRONJ. **Results:** There were 126 responses to the survey conducted. Majority (87%) of responders were dentists in private, including group dental practices, with 74% having more than 11 years of working experience. Most (81%) have not had any encounters with patients with MRONJ. The pre-lecture survey showed that 60% of responders expressed slight or no confidence at all in treating patients who are on osteoporosis treatment. Only 19% of all responders were able to correctly identify the risk of MRONJ in patients on osteoporosis treatment. Majority of responders tended to inflate MRONJ risk by as much as 100 times the quoted baseline risk in the literature. One third of dentists would not perform any invasive treatments on patients on osteoporosis treatment. Post-lecture, the percentage of responders with slight and no confidence at all in treating patients who are on osteoporosis treatment decreased to 18%. 65% of responders were able to correctly identify the risk of MRONJ in patients on osteoporosis treatment as quoted in the literature. Only 3% of dentists would not perform any invasive treatments on patients on osteoporosis treatment. 95% of responders correctly stated that maintenance of good oral hygiene is the most important measure to prevent MRONJ. Attendees suggested the creation of a joint guidance from local osteoporosis and dental societies may better improve knowledge and instill confidence in treating osteoporosis patients. **Conclusion:** There is a significant knowledge gap within the dental practitioners in Singapore on the risk of MRONJ associated with osteoporosis treatments. This may result in dentists discouraging patients from starting osteoporosis