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Genetic Screening of ZNF687 and PFN1 in a Paget's Disease of Bone Cohort Indicates an Important Role for the Nuclear Localization Signal of ZNF687
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Abstract
Paget's disease of bone (PDB) is a common, late-onset bone disorder, characterized by focal increases of bone turnover that can result in bone lesions. Heterozygous pathogenic variants in the Sequestosome 1 (SQSTM1) gene are found to be the main genetic cause of PDB. More recently, PFN1 and ZNF687 have been identified as causal genes in patients with a severe, early-onset, polyostotic form of PDB, and an increased likelihood to develop giant cell tumors. In our study, we screened the coding regions of PFN1 and ZNF687 in a Belgian PDB cohort (n = 188). In the PFN1 gene, no variants could be identified, supporting the observation that variants in this gene are extremely rare in PDB. However, we identified 3 non-synonymous coding variants in ZNF687. Interestingly, two of these rare variants (p.Pro937His and p.Arg939Cys) were clustering in the nuclear localization signal of the encoded ZNF687 protein, also harboring the p.Pro937Arg variant, a previously reported disease-causing variant. In conclusion, our findings support the involvement of genetic variation in ZNF687 in the pathogenesis of classical PDB, thereby expanding its mutational spectrum. © 2023, The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature.

Author Keywords
Mutation analysis; Paget's disease of bone; PFN1; Profilin 1; ZNF687

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