عنوان المشروع باللغة العربية	العلاقة بين اختلافات في جينWNT16 و هشاشة العظام بعد سن اليأس في السعودية
عنوان المشروع باللغة الإنجليزية	Association of WNT16 Gene variants With Osteoporosis in Post-menopausal Saudi Subjects
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المدة المتوقعة لإنجاز البحث منذ الحصول على موافقة عمادة الدراسات العليا	شهر 12
Abstract or synopsis of the proposal (200 words or less):	Osteoporosis is a complex common disease characterized by low bone mineral density (BMD), deterioration in bone microarchitecture, and an increased risk of fracture [1]. Susceptibility to osteoporosis depends on both genetic and environmental determinants. Twin and family studies have shown the gen etic contribution to different traits related to osteoporosis (2). Recent genome wide association studies (GWAS) and candidate gene studies have identified strong association of WNT16 gene with BMD, hip geometry parameters, fracture risk, and bone acquisition (2).The WNT16 gene is located on chromosome 7q31.31, codes for a protein belonging to the Wnt family, which is known to regulate bone homeostasis [3]. The importance of Wnt16 in the regulation of bone metabolism has been confirmed in Wnt16 (Wnt16−/−) knockout (KO) mouse models [2]. Four single nucleotide polymorphisms (SNPs) (rs2908004, rs2908007, rs2707466 and rs3801387) in WNT16 were shown to be associated with BMD and broadband ultrasound attenuation measurement in Caucasian individuals, suggesting that WNT16 influences bone mass (4).
Hypothesis or scientific justification of the proposal	Based on the above findings, it will be interesting to study the impact of WNT16 SNPs on osteoporosis risk and to verify whether such SNPs could influence BMD in post-menopausal Saudi subjects. The Polymorphism at specific loci in WNT16 gene can serve as genetic contributor for low BMD and risk of osteoporosis.
Specific objectives	1). To test the genotype and allelic frequencies of WNT16 gene variants (rs2908004, rs2908007, rs2707466 and rs3801387) in subjects with and

	without osteoporosis. 2). To investigate the association between WNT16 gene variants and occurrence of osteoporosis in post-menopausal Saudi subjects. 3). To study the haplotype frequencies of the rs2908004, rs2908007, rs2707466 and rs3801387 in WNT16 gene with the risk of osteoporosis. 4). To correlate WNT16 gene variants with BMD and serum bone markers.
Methodology & Major Techniques to be used	Post-menopausal osteoporotic Saudi subjects (N = 100) and an equal number of age matched controls will be recruited for the study. Anthropometry included height (rounded off to the nearest 0.5 cm), weight (rounded off to the nearest 0.1kg), waist and hip circumference (centimeters), and mean systolic and diastolic blood pressure (millimeters of Hg) (average of 2 readings). Body mass index (BMI) will be calculated as weight in kilograms divided by height in square meters. Diagnosis of osteoporosis will be based T-score measured by DEXA. The subjects with T-score below -2.5 will be considered as osteoporotic and those with T-score above -1 will be considered as control. Fasting blood samples will be collected and transferred immediately to a non-heparinized tube for centrifugation. Fasting glucose and lipid pr ofile will be measured using a chemical analyzer (Konelab, Espoo, Finland). Serum bone markers (osteocalcin and N-Tx will be assessed using an enzyme-linked immunosorbent assay (ELISA). Genotyping Genomic DNA will isolated from whole blood using the blood genomicPrep mini spin kit (GE healthcare Life Sciences, Piscataway, NJ, USA). DNA concentration and purity (260/280) will checked using Nano-drop spectrophotometer. The four tagging SNPs (rs2908004, rs2908007, rs2707466 and rs3801387) in WNT-16 gene will be evaluated by allelic discrimination Real-time PCR using pre-designed TaqMan genotyping assays from Applied Bio-systems (Foster City, CA, USA). Major Techniques: (i) DNA extraction (ii) Measurement of Biochemical parameters. (iii) SNP detection using allelic discrimination real-time PCR (iv) ELISA
Availability of	YES

Samples	
If the answer is no, kindly justify	
Availability of Chemicals	YES
If the answer is no, kindly justify	
Availability of Instruments	YES
Availability of Ethical Approval (if needed)	YES
Recent References	1. Genant HK, Cooper C, Poor G, Reid I, Ehrlich G, Kanis J, Nordin BC, Barrett-Connor E, Black D, Bonjour JP, Dawson-Hughes B. Interim report and recommendations of the World Health Organization task-force for osteoporosis. Osteoporosis International. 1999 Sep 20;10(4):259-64. 2. Correa-Rodríguez M, Rio-Valle JS, Rueda-Medina B. Polymorphisms of the WNT16 gene are associated with the heel ultrasound parameter in young adults. Osteoporosis International. 2015 Oct 28:1-5. 3. Logan CY, Nusse R. The Wnt signaling pathway in development and disease. Annu. Rev. Cell Dev. Biol.. 2004;20:781-810. 4. Garcia-Ibarbia C, Perez-Nunez MI, Olmos JM, Valero C, Perez-Aguilar MD, Hernandez JL, Zarrabeitia MT, González-Macías J, Riancho JA. Missense polymorphisms of the WNT16 gene are associated with bone mass, hip geometry and fractures. Osteoporosis International. 2013 Sep 1;24(9):2449-54.