عنوان المشروع باللغة العربية	
عنوان المشروع باللغة الإنجليزية	**Effect of Vitamin D Binding Protein polymorphisms and vitamin D supplementation on serum vitamin D concentration in Saudi T2DM subjects**
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التخصص الدقيق للمشرف الرئيس	البيولوجية الجزيئية
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المدة المتوقعة لإنجاز البحث منذ الحصول على موافقة عمادة الدراسات العليا	12 شهر
Abstract or synopsis of the proposal (200 words or less):	T2DM is a metabolic disorder characterized by hyperglycemia and insulin deficiency; this disease recognizes a multifactorial pathogenesis in which genetic factors play a complex and yet not clearly defined role (1). Vitamin D insufficiency has been increasingly recognized as a common health problem worldwide. During the recent years, there has been accumulating evidence from various interventional studies on the beneficial effects of improving vitamin D status among patients with DMT2 (2). Vitamin D metabolites in the circulation are bound to vitamin D binding protein (DBP) encoded by a highly polymorphic gene GC. The GC is located on chromosome 4q13 and has 13 exons encoding 474 amino acids. There are two common functional single nucleotide polymorphisms (SNPs) in exon 11 of GC, which are rs4588 and rs7041 positioned at codons 416 and 420 (3). Based on these findings, it was decided to study the impact of SNPs in DBP on diabetes risk and to verify whether such SNPs could influence circulating serum Vitamin D concentration in the Saudi population. However, no such associations have been examined in the Saudi population, despite the high incidence of Vitamin D deficiency in Saudi Arabia.
Hypothesis or	Little is known about the genetic epidemiology of vitamin D that

scientific justification of the proposal	appears to be vitally important to our health. Thus, we would like to investigate whether the genetic variants in Vitamin D binding protein has any influence on vitamin D responsiveness.
Specific objectives	1. To determine if allelic variants of the DBP gene affect the response to vitamin D supplementation. 2. To measure the serum levels of Vitamin D in subjects with T2DM and control subjects and correlate with DBP genotypes.
Methodology & Major Techniques to be used	**Subject selection and biochemical analyses** Saudi T2DM subjects between the ages of 35-60 years (N = 100) and an equal number of age matched controls will be recruited for the study. Anthropometry including 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) will be measured. Body mass index (BMI) will be calculated as weight in kilograms divided by height in square meters. Fasting blood samples will be collected and transferred immediately to a non-heparinized tube for centrifugation. Fasting glucose and lipid profile will be measured using a chemical analyzer (Konelab, Espoo, Finland). Serum levels of Vitamin D will be assessed using an enzyme-linked immunosorbent assay (ELISA). **Genotyping** Genomic DNA will be isolated from whole blood using the blood genomic Prep mini spin kit (GE healthcare Life Sciences, Piscataway, NJ, USA). DNA concentration and purity (260/280) will be checked using Nano-drop spectrophotometer. The two tagging SNPs (rs4588 and rs7041) in DBP 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 Samples	Yes
Availability of Chemicals	Yes
Availability of Instruments	Yes
Availability of Ethical Approval (if needed)	Yes
Recent References	1. Al-Daghri, Nasser M., Omar Al-Attas, Majed S. Alokail, Khalid M. Alkharfy, Hossam M. Draz, Cristina Agliardi, Abdul Khader Mohammed, Franca R. Guerini, and Mario Clerici. "Vitamin D receptor gene polymorphisms and HLA DRB1* 04 cosegregation in Saudi type 2 diabetes patients." *The Journal of Immunology* 188, no. 3 (2012): 1325-1332. 2. Al-Daghri, Nasser M., Hanan Alfawaz, Naji J. Aljohani, Yousef Al-Saleh, Kaiser Wani, Abdullah M. Alnaami, Mohammad Alharbi, and Sudhesh Kumar. "A 6-month “self-monitoring” lifestyle modification with increased sunlight exposure modestly improves vitamin D status, lipid profile and glycemic status in overweight and obese Saudi adults with varying glycemic levels." *Lipids in health and disease* 13, no. 1 (2014). 3. Nimitphong, Hataikarn, Sunee Saetung, Suwannee Chanprasertyotin, L. O. Chailurkit, and Boonsong Ongphiphadhanakul. "Changes in circulating 25-hydroxyvitamin D according to vitamin D binding protein genotypes after vitamin D3 or D2 supplementation." *Nutr J* 12, no. 1 (2013): 39.