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عنوان المشروع باللغة العربية - Title of the proposed project in Arabic

تعرف على طفرات جين ABCC8 المسؤولة عن مرض السكري في حديثي الولادة في السعودية.

Title of the proposed project in English

Identification of the mutations in ABCC8 gene responsible for the neonatal diabetes in Saudi population

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المدة المتوقعة لإنجاز البحث منذ الحصول على موافقة عمادة الدراسات العليا (بالشهور) - Expected time in month to finish

شهر 12

Abstract of the proposal (No more than 200 words)

The mutations in the ABCC8 gene are the most common cause of neonatal diabetes which is typically diagnosed in the first six months of life. The pathogenic mutations in this gene have been extensively studied in neonates or infants less than age of 6 months. Literature survey revealed that postnatal genetic screening of Saudi neonates and infants has never been studied

previously. Therefore, current study is designed to investigate the pathogenic mutations and polymorphisms in Saudi neonates and infants. For current study blood samples from infants with age less than 6 months and new born babes with postnatal age of 3 days will be collected. Selected mutations in collected samples will be studied by SNP Genotyping and sanger sequencing. This study will be first step toward the establishment of nationwide neonatal diabetes genetic screening program in Saudi Arabia. Hence, studying mutations in neonates will be helpful for future treatment, control and prevention of the diabetes in Saudi population.

### **Hypothesis of the proposal**

- This study will help to find frequency of certain mutations in diabetes associated genes in Riyadh, KSA.
- This study will help to screen out the carrier individuals that will help to develop prenatal diagnosis and genetic counseling strategies to prevent genetic diabetes in Saudi population.
- Moreover, through seeking pre implantation genetic diagnosis (PGD), families with known mutations may have the possibility of having children free from those mutations.
- An identification of the ABCC8 mutations has important therapeutic implications for patients; mutations carriers can switch from insulin injections to oral sulfonylurea, which results in improved glycemic control.
- This study will help to establish the basis for the nationwide genetic diagnosis program for neonatal diabetes.

### **Specific objectives**

- To identify the mutations in ABCC8 gene causing neonatal diabetes in Saudi population.
- To investigate the frequency of ABCC8 mutations and association with other factors in Saudi neonates and infants.
- Genetic counselling of the parents for prevention and control of the genetic diabetes.

### **Methodology & Major Techniques to be used**

Blood Sampling:

Blood samples from umbilical cord will be collected in EDTA tubes from the neonates at the time of birth or 3-4 drops of blood will be collected by heel puncture at sterilized filter papers. For some cases (age less than 6 months) 0.5-1cc venous blood in EDTA tubes may also be collected. Sampling will be performed at different hospitals of the Riyadh. After collection samples will be stored in -20 °C before DNA extraction.

DNA extraction:

Genomic DNA will be extracted by using Qiagen Genomic Extraction kits, which simply employ spin columns, for the isolation of DNA. The spin columns contain a silica resin that selectively binds DNA, depending on the salt conditions and other factors influenced by the extraction method.

Genetic screening:

Pathogenic mutations/polymorphisms neonatal diabetes associated in ABCC8 gene will be investigated by SNP Genotyping Analysis Using TaqMan Assays. Special fluorescent probed primers will be designed and amplified by realtime PCR (Applied Biosystems, Foster City, CA). For results validation and confirmation, the identified mutations/polymorphisms will further be analyzed by Sanger sequencing methods. For this purpose, special primers will be designed for each of the targeted mutations, which will be amplified by conventional thermocycler (Applied Biosystems, Foster City, CA). The amplicons will be precipitated with ethanol and sequenced with Big Dye Terminator version 3.1 (Applied Biosystems, Foster City, CA). Sequenced samples will be electrophoresed on an ABI 3730 genetic analyzer, and the traces will be inspected by SeqMan software (DNASTar Lasergene version 5.0.221.0).

**Availability of Samples**

Yes

**Availability of Chemicals**

Yes

**Availability of Instruments**

Yes

**Ethical Approval**

Ethical approval is available

**Recent References**

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