ملخص مشروع رسالة ماجستير-٢

عنوان المشروع باللغة العربية	المؤشرات الحيوية المحتملة لنشاط أنزيم كارنتين بالميتويل ترانسفيراز الأول والثاني وتطبيقاتهما المرضية في مصل الدم لدى مرضى إحتشاء عضلة القلب الحاد
English /عنوان المشروع باللغة الإنجليزية	Biomarker potential of serum carnitine palmitoyltransferase-I B (CPT1B) and carnitine palmitoyltransferase-2 (CPT2) enzyme activities for disease stratification in acute myocardial infarction
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Minor /التخصص الدقيق للمشرف الرئيس Specification	Enzymes and Medical Biochemistry
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المدة المتوقعة لإنجاز البحث منذ الحصول على موافقة عمادة الدراسات العليا	10-12 months
Abstract or synopsis of the proposal (200 words or less):	Acute myocardial infarction (AMI), commonly known as heart attack is an irreversible necrosis of the heart muscles secondary to prolonged ischemia. AMI is a major public health problem worldwide. Its rapid and precise diagnosis as well as risk stratification is of great significance to enable immediate and intensified treatment which consequently reduces mortality. Recent studies have shown rising incidence of AMI in young generation of Saudi Arabia. Carnitine (3-hydroxy-4-N-trimethylammonium butyrate) is an essential cofactor in fatty acid metabolism. Carnitine palmitoyltransferase I (CPT1) in the outer surface of inner mitochondrial membrane transfers acyl group from acyl CoA to carnitine forming acylcarnitine. There are 3 isoforms of CPT1; of these, CPT1B is highly expressed in heart and skeletal muscle cells. Another enzyme, CPT2, located in the inner surface of the inner mitochondrial membrane, removes the acyl group from acylcarnitine and transfers it to CoA to form acyl CoA in the mitochondrial matrix. Recently, we have reported 4 novel variants in CPT1B gene and 2 variants in CPT2 gene. We have also shown significantly high blood carnitine levels in AMI patients as compared to controls while

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	some variants of CPT1B and CTP2 genes had altered carnitine levels. However, alteration in serum CPT1B and CPT2 enzymes activities in AMI patients is still a matter of investigation.
Hypothesis or scientific justification of the proposal	Both CPT1B and CPT2 enzymes play an important role in carnitine homeostasis. Previously we have shown that blood carnitine levels are significantly increased in AMI patients. One possible explanation to this carnitine increase was attributed to reduced uptake and/or increased leakage of carnitine from ischemic myocardium. An alternate hypothesis could be associated with altered activities of the enzymes governing the transport of fatty acids into mitochondria using carnitine-acylcarnitine system. If the latter hypothesis is true, the activities of CPT1B and CPT2 enzymes could be utilized as potential biomarker for AMI in high risk individuals. We will test the hypothesis by examining the correlations between blood carnitine and the relevant enzymes activities.
Specific objectives	(1) To determine the CPT1B and CPT2 enzyme activities in the sera of AMI patients and controls (2) To study the correlation between these enzymes and other cardiac markers as well as patients characteristics.
Methodology and Major Techniques to be used	Serum samples from AMI patients and control subjects will be analyzed for CPT1B and CPT2 enzyme activities using enzyme linked immunosorbent assay (ELISA). The microtiter plate provided in the kit has been pre-coated with an antibody specific to the target enzyme. Standards or samples are then added to the appropriate microtiter plate wells with a biotin-conjugated antibody specific to target enzyme. Next, Avidin conjugated to Horseradish Peroxidase (HRP) is added to each microplate well and incubated. After TMB substrate solution is added, only those wells that contain the target enzyme, biotin-conjugated antibody and enzyme-conjugated Avidin will exhibit a change in color. The enzyme-substrate reaction is terminated by the addition of sulphuric acid

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	solution and the color change is measured spectrophotometrically at a wavelength of 450 nm. The concentration of enzyme in the samples is then determined by comparing the absorbance of the samples to the standard curve. The enzyme levels will be correlated with blood carnitine levels, cardiac markers and patient characteristics. Data will be analyzed by analysis of variance followed by Dunnett's test and Pearson's test. P values less than 0.05 will be considered as statistically significant.
Availability of Samples	YES ◉ NO ○
Availability of Chemicals	YES ◉ NO ○
Availability of Instruments	YES ◉ NO ○
Availability of Ethical Approval (if needed)	YES ○ NO
Project Funded	YES ○ NO
Recent References	1. Khan HA, Alhomida AS, Al Madani H, Sobki SH. Carnitine and acylcarnitine profiles in dried blood spots of patients with acute myocardial infarction. Metabolomics 2013; 9 (4): 828-838. 2. Khan HA, Alhomida AS. Single nucleotide polymorphism in CPT1B and CPT2 genes and its association with blood carnitine levels in acute myocardial infarction patients. Gene 2013; 523(1): 76-81. 3. Khan HA, Alhomida AS, Sobki SH. Lipid profile of patients with acute myocardial infarction and its correlation with systemic inflammation. Biomarker Insight 2013; 8: 1-7. 4. Khan HA, Alhomida AS, Rammah TY, Sobki SH, Ola MS, Khan AA. Alterations in prothrombin time and activated partial thromboplastin time in patients with acute myocardial infarction. Int J Clin Exp Med 2013; 6: 294-297. 5. Khan HA, Alhomida AS, Sobki SH, Al Moghairi A, El Koronki H. Blood cell

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	counts and their correlation with creatine kinase and C-reactive protein in patients with acute myocardial infarction. Int J Clin Exp Med 2012; 5 (1): 50-55. 6. Khan HA, Alhomida AS, Sobki SH, Al Moghairi A. Significant increases in monocyte counts and serum creatine kinase in acute myocardial infarction versus general infections. Ind J Pathol Microbiol 2012; 55 (4): 474-477. 7. Islam S, Yakout SM, Al Daghri NM, Alhomida AS, Khan HA. Serum levels of thrombotic markers in patients with acute myocardial infarction. Int J Clin Exp Med 2014; 7(4): 1059-1063.