عنوان المشروع باللغة العربية	العلاقة بين عدم إستقرار التتابعات الصغيرة المتكررة و التعبير الجيني لمورثات إصلاح عدم التوافق في عينة من مرضى سرطان القولون السعوديين
عنوان المشروع باللغة الإنجليزية	Correlation between Microsatellite Instability Status and the Expression of Mismatch repair Genes in a sample of Saudi Colon Cancer patients
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التخصص الدقيق للمشرف الرئيس	بروتينات و احياء جزيئية
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المدة المتوقعة لإنجاز البحث منذ الحصول على موافقة عمادة الدراسات العليا	12
Abstract or synopsis of the proposal (200 words or less):	Colorectal cancer is one of the most common forms of cancer in Western countries. In most cases, these cancers are seen sporadically, bu t 5 to 10 % of cases are associated with a primary genetic factor. Hereditary nonpolyposis colorectal cancer (HNPCC) is secondary to an inherited mutation in one of the deoxyribonucleic acid (DNA) MMR genes (hMLH1, MLH3, hMSH2, hMSH3, hMSH6, and hPMS2). 1, 2 Indeed, MMR system is necessary for the diagnosis and correction of insertion or deletion errors and mismatches in DNA that occur during DNA replication. In tumors that develop due to defective DNA mismatch repair, repetitive DNA sequences known as microsatellites tend to undergo a high level of genetic alteration, resulting in MSI. By molecular biology, microsatellite instability is classified according to the level of instability detected as high (MSI-H), low (MSI-L), or stable (MSS).3 Clinically, the MSI cancers are more often located in the proximal colon (right and transversal). Moreover, MSI-H cancers have a better prognosis than spontaneous MSI-L and MSS, regardless of tumor stage cancers. 4 They are associated wi th a lower risk of metastasis. To the best of our knowledge, there is a little information on MMR expression profile in Saudi patients with CRCs. So, in the current study, we intended to evaluate microsatellite instability pattern and its relationship with expression of MMR pathway genes (MLH1, MLH3, and MSH6), in a cohort of Saudi Arabian patients with CRCs. MSI and MSS colon cancer samples will be screened to quantify gene expression levels and determine whether differences exist between MSI and MSS patients.
Hypothesis or scientific justification of the proposal	The microsatellite instability (MSI) pathway is found in most cases of hereditary nonpolyposis colorectal cancer (HNPCC) and in 12 % of sporadic colorectal cancer (CRC). It involves inactivation of deoxyribonucleic acid mismatch repair (MMR) genes MLH1, MLH3, PMS2, and MSH6. MMR germline mutation detections are an important supplement to HNPCC clinical diagnosis. Indeed, MMR system is necessary for the diagnosis and correction of insertion or deletion errors and mismatches in DNA that occur during DNA replication. In tumors that develop due to defective DNA mismatch repair, repetitive DNA sequences known as microsatellites tend to

	undergo a high level of genetic alteration, resulting in MSI. 4 To the best of our knowledge, there is a little information on MMR expression profile in Saudi patients with CRCs. So, in the current study, we intended to evaluate microsatellite instability and gene expression pattern of MMR pathway genes and its relationship to clinicopathological findings (MSI and MSS), in Saudi patients with CRCs.
Specific objectives	The present case-control based study was performed to investigate the role of microsatel lite instability and MMR pathway genes in developing colorectal cancer risk in Saudi colorectal cancer patients. The main aims of the present study are: 1. Analysis Saudi colorectal cancer samples for microsatellite instability. 2. Screening of MSI and MSS colon cancer samples to quantify gene expression in MMR pathway genes to determine whether differences exist between MSI and MSS patients.
Methodology & Major Techniques to be used	
Availability of Samples	YES
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. Kim, Tae-Min, Peter W. Laird, and Peter J. Park. "The landscape of microsatellite instability in colorectal and endometrial cancer genomes." Cell 155.4 (2013): 858-868. 2. Bogaert, Julie, and Hans Prenen. "Molecular genetics of colorectal cancer." Annals of Gastroenterology 27.1 (2014): 9. 3. Giedl, Johannes, et al. "Low Frequency of HNPCC-Associated Microsatellite Instability and Aberrant MMR Protein Expression in Early-Onset Bladder Cancer." American journal of clinical pathology 142.5 (2014): 634. 4. Amira, Arfaoui Toumi, et al. "Immunohistochemical expression pattern of MMR protein can specifically identify patients with colorectal cancer microsatellite instability." Tumor Biology 35.7 (2014): 6283-6291.