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Analysis and quantification of microRNAs in prostate tumors

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Registration date 28/05/2013	**Overall study status** Completed	
Last Edited 01/09/2020	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
In Europe prostate cancer is the most common solid cancer and the third leading cause of cancer death in men. miRNAs are small molecules that control various body processes and are found in different amounts in tumour cells compared to normal cells. Recent studies have shown that abnormal levels of miRNAs contribute to the development of cancer. They could be used as markers to provide diagnostic information (identifying the nature of the cancer) and prognostic information (predicting the likely course of the cancer). The aim of this study is to assess the levels of miRNAs in prostate tumours.

Who can participate?
Patients aged over 18 with prostate cancer, and healthy volunteers

What does the study involve?
Participants provide blood samples which are tested to find miRNAs that are present at high or low levels in prostate tumours, which could be used in the diagnosis and prognosis of prostate cancer.

What are the possible benefits and risks of participating?
The results of this study will help with the search for new markers that will benefit patients with cancer in the future. There are no risks of participating in this study.

Where is the study run from?
Hospital A Coruña (Spain)

When is the study starting and how long is it expected to run for?
March 2011 to June 2015

Who is funding the study?
The Foundation for Research in Urology (Beca Fundación para la Investigación en Urología) (Spain)

Who is the main contact?
Dr Francisco Gómez-Veiga

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Analysis and quantification of microRNAs in prostate tumors: an observational study

Study objectives
Cancer is essentially a genetic disease characterized by an uncontrolled proliferation and survival of damaged cells, resulting in tumor development. Prostate cancer is one of the main pathologies that must deal with the male population. In Europe we can state that it is the most common solid neoplasm followed by lung and colorectal cancer and the third leading cause of cancer death in men. We possess different predictive factors for this disease with the purpose to establish a prognosis and tailor the therapeutic strategies. However, the prognostic capacity of these parameters is limited and can be enhanced with the incorporation of other factors. In this sense, the miRNAs, small molecules that regulate various biological processes (division, differentiation, apoptosis, and metabolism) which have recently been involved in the development of cancer. Therefore, if the miRNAs are involved in oncogenesis, inflammatory response or other disease states, the expression studies of these RNAs of small size may reveal new diagnostic or prognostic markers.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Ethics board: Clinical Research Ethics Committee of Galicia [Comité Ético de Investigación Clínica de Galicia (CEIC)], 29/03/2011

Study design
Observational study of cases and controls

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Prostate cancer

Interventions
1. Sample Collection: Peripheral blood samples will be collected into tubes containing EDTA with the sole precaution of discarding the first milliliters to avoid possible contamination of samples with epithelial cells which may subsequently interfere with the results.
2. Data collection and analysis: Data of usual clinical and prognostic variables (age, TNM-AJCC stage, location of primary sites of metastatic disease, hormone receptor status, degree of differentiation, etc.) will be collected at the time of inclusion of the patient, through a data collection form designed specifically for the study. Blood samples will be coded and specific data (volume obtained PCR results Real Time PCR, etc.) will be collected and analyzed separately from the clinical data. All variables will be stored in a computer database.
3. Finding differentially expressed miRNAs candidates: A computer support will be used in addition to the literature search on the website of the National Center for Biotechnology Information http://www.ncbi.nlm.nih.gov/entrez/query.fcgi) through free access databases of miRNAs on the following pages and others: http://mirnamap.mbc.nctu.edu.tw/;http://microrna.sanger.ac.uk/;http://www.ma.uniheidelberg.de/apps/zmf/argonaute/interface/. These pages are being updated constantly and are very useful for finding potential markers of miRNA (microRNA) that may be over-expressed or under-expressed in prostate tumors.
4. RNA extraction, PCR arrays, RT-PCR and real-time PCR (qRT-PCR): Once we get a panel of potential miRNA markers in blood of patients with prostate tumors, specific primers will be designed and to confirm the sensitivity of these studied its expression will be checked by RT-PCR in real time once the conditions are optimized for each microRNAs.
5. Biostatistical analysis of the results: The process of data normalization is essential for a correct process of quantifying the levels of microRNA here. Usually the method used in the standardization process is the use of a housekeeping gene. But in the case of miRNAs are still insufficient data which can be used as endogenous controls, so that expression data are normalized after selecting through the literature and verified by GENEX software (fine Analyser) those with more stable expression. The relative quantification of the expression of miRNAs will be calculated using the Genex software (fine Analyser) from the average log of expression of all the samples studied. The data will be analyzed using the viewer Multiexperiment programs TIGR version 4.6.1 (available in http://www.tm4.org/mev.html) and SPSS PASW Statistics 19. To identify miRNA with significantly different expression between different groups, multivariate analysis of permutations: Significance Analysis of Microarrays (SAM) with a False Discovery Rate <10%. The Analysis of Microarrays Prediction (MAP) will be used to identify those miRNAs that will be able to classify a sample into one group or another of those tested. Thus, by this analysis we will reduce the group of miRNA in importance according to the characteristics studied. The

relationship between the positivity of the markers and clinical variables of interest will be studied using Chi-square test and logistic regression analysis in case of relative risks. The quantitative results will be compared using parametric statistics, unless the distribution of the variable results of studies advice the use of nonparametric statistics. Finally, we will conduct a study of time to progression and disease-free survival in such a way as to organize follow up patients for 5 years. We will make the relevant Kaplan Meier curves and to analyze their statistical significance log rank test will be used. Multivariate analysis will be performed using Cox's test, which will allow prognostic independence of the variables in study.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
1. Look at the possible relationship between the expression profiles of the microRNAs and the ability of prediction groups risk in prostate cancer, in patients who have not suffered therapeutic maneuvers
2. Establish a panel of circulating microRNAs useful in the diagnosis and prognosis of prostate cancer

Key secondary outcome(s))
1. We will explore different patterns of microRNAs to estimate the response to the local therapy or hormonal manipulation including in the context of hormone-refractory patients
2. Identification of potential target genes of the microRNAs with significance by predictions of interaction through the mirbase database, TargetScan and the software's Crosslink and Pathway Studio (Ariadne Genomics)

Completion date
30/06/2015

Eligibility

Key inclusion criteria
1. Patients with pathological diagnosis confirmed of localized, locally advanced or metastatic prostate cancer according to the TNM (tumor, lymph nodes, metastasis) classification, NCCN (National Comprehensive Cancer Network), during the period of study
2. Older than 18 years
3. Patients with signed informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Male

Key exclusion criteria
1. Patients with a history of epithelial cancer, except skin carcinoma correctly treated
2. Patients who are receiving systemic cancer treatment
3. Thrombocytopenia less than 20,000 /ml or coagulopathies not medically controlled

Date of first enrolment
29/03/2011

Date of final enrolment
30/06/2015

Locations

Countries of recruitment
Spain

Study participating centre
CHU A Coruña
A Coruña
Spain
15006

Sponsor information

Organisation
The Foundation for Research in Urology [Fundación para la Investigación en Urología (FIU)] (Spain)

Funder(s)

Funder type
Charity

Funder Name
The Foundation for Research in Urology (Beca Fundación para la Investigación en Urología) (Spain) 2010-2012

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results		11/05/2012		No	No
Abstract results		20/05/2013		No	No
Abstract results		10/11/2018		No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes