FAMILIAL CANCER CLINICAL UNIT

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OVERVIEW

Individuals that present with an uncommon malignancy or with cancer at an early age of onset deserve special attention because they are more likely to harbour an inherited predisposition and may require unique treatment strategies. Identification of a heritable cancer predisposition syndrome is not only essential for genetic counselling and for the design of a surveillance scheme for both the patient and his/her relatives, but also for facilitating the refinement and optimisation of treatment strategies so as to minimise toxicity and maximise efficacy. Vigilance of these syndromes can significantly enhance the quality and comprehensiveness of clinical management of cancer.

In addition, the evaluation of inherited cancer predisposition is changing with the routine use of NGS. Despite the promise of NGS, the utility of testing multiple genes with different modes of inheritance and with varying levels of penetrance has been questioned due to the increasing costs of surveillance and unnecessary treatments, and the uncertain consequences of the identification of variants of unknown significance. More than ever it is necessary to underline that NGS testing should only be offered in the context of expert genetic counselling.

In the Cancer Genetics Consultation of the Familial Cancer Clinical Unit (FCCU) we work together with Fuenlabrada Hospital clinicians, as well as health-care providers from other Madrid hospitals and other Autonomous Communities, in order to heighten the vigilance of hereditary cancer syndromes and to better adapt the genetic counselling process in alignment with the introduction of new technologies.

CLINICAL, DIAGNOSTIC AND RESEARCH HIGHLIGHTS

The FCCU evaluates individuals and families who are at an increased risk of developing cancer at our cancer genetics consultancy in the Medical Oncology Service of the *Hospital Universitario de Fuenlabrada* (HUF). The referral system, surveillance and treatment measures are discussed with medical oncologists and other clinicians during the monthly sessions conducted by the hospital's Hereditary Cancer Clinical Committee. During 2016, our consultancy at HUF was visited by 408 patients, a 21% increase over 2015. Moreover, 352 genetic diagnostic studies were performed in the FCCU laboratory (306 in 2015). We also tested patients with multiple gene panels; this enables us to offer results on genes of interest in just a few weeks' time. The FCCU has continued to actively contribute to unravel the complexity of genetic cancer predisposition and to help refine tools for a better evaluation of patients and families. FCCU members collaborate with the 'Lynch Syndrome prediction model validation study group' to define the most precise tools for the evaluation of families with hereditary colorectal cancer as well as to identify the best candidates for genetic studies. In collaboration with other research groups, the FCCU has defined the role of the *UNC5C* gene in hereditary forms of colorectal cancer and in polyposis, as well as the role of *OGG1* as a cancer risk modifier in *BRCA1* and *2* mutation carriers.

Genetic susceptibility to colorectal cancer is a key area focus for the FCCU's research activities. Familial or hereditary forms of colorectal cancer, early-onset colorectal cancer (EOCC), and synchronous or metachronous colorectal tumours are our main topics of interest. We have continued the characterisation of EOCC, on the premise that the carcinogenetic mechanism and the progression of these tumours may differ in comparison with late-onset colorectal cancer (LOCC) (FIGURE). The *APC* gene status, wild-type or mutated, seems to be a marker of prognosis in colorectal cancer with microsatellite stability (MSS), but the prognosis would have a different sign in EOCC and LOCC. In MSS-EOCC, the worst prognosis was associated with *APC*-mutated tumours and distal location. However, in the MSS-LOCC group, the worst prognosis was observed among proximally located tumours with *APC*-wild type. These results not only continue to suggest a different behaviour according to the age of onset, but also define different groups in relation to the tumour location.

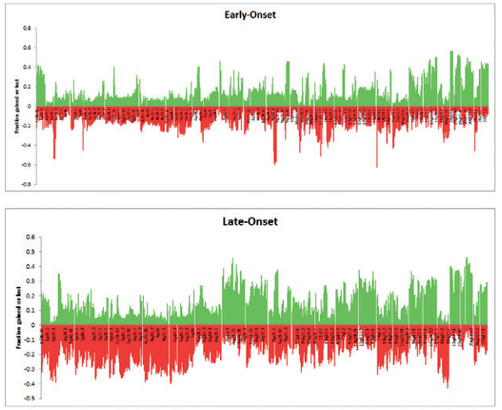

Figure Copy number gains and losses in ≤45 y-o and ≥70 y-o colorectal cancers.

During 2016 the FCCU has maintained a fruitful relationship with *AEAS*. Several members of the association have received genetic counselling in our consultancy, and the study of sarcoma predisposition genes (mainly *TP53*, *POT1* and *CDKN2A*) was also carried out in our laboratory. These activities are part of our ongoing collaborations with cancer patients associations. Recently, we have designed a new survey that will be distributed among members of the *AEFAT* with the aim of identifying those families with an increased susceptibility to cancer. ■

PUBLICATIONS

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Book chapter

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PATENT

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