UTILITY OF FLUORESCENCE IN SITU HYBRIDISATION (FISH) IN DIAGNOSIS AND THERAPY OF OCULAR MELANOCYTIC LESIONS

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Background and aims of the project:

A first aim of the project is to determine the role of c-KIT gene amplification in uveal melanocytic lesions. Since there is a targeted designed treatment directed against c-KIT (by STI571 or Imatinib), this part of the study can have important therapeutic implications for uveal melanocytic lesions.
The second part of the study uses 4 FISH probes that have been proven to be of diagnostic value in cutaneous melanoma and that help in determining whether these lesions are either benign or malignant. This project will study the role of these 4 melanoma FISH probes in the diagnosis of conjunctival melanocytic lesions. This could be helpful in determining lesions that are difficult to classify based on pathologic examination, such as Primary Acquired Melanosis (PAM).

Development of the project:
The first part of the study emphasizes on c-KIT gene amplification in uveal melanocytic lesions.

c-KIT is a proto-oncogene that plays an important role in the development of several tumours (such as gastro-intestinal stromal tumours = GIST, seminomas, cutaneous melanomas, mastocytosis,...). Moreover, a designed therapy with STI571 (Imatinib) exists, specifically targeted against the c-KIT tyrosine kinase. This treatment has been proven to be very effective in GIST tumours.

Little is known about the role of the c-KIT proto-oncogene in uveal melanomas. Several studies suggest a possible important role of the c-KIT protein and the ligand Stam Cell Factor (SCF) in uveal melanomas. Amplification of the gene however, hasn't been studied yet. Amplification is an important oncogenic mechanism in several tumours.

The aim of the first part of the project is to try and detect amplification in the c-KIT gene in uveal melanomas, using a Fluorescence In Situ Hybridisation (FISH). This test will be performed on specimens of excised (enucleated) uveal lesions (melanomas and naevi), using a homemade c-KIT probe. As such amplification or polyploidy will be studied.

The second part of the project uses 4 FISH probes to determine conjunctival melanocytic lesions. These probes have been proven to be of diagnostic value in cutaneous melanomas. The aim is to study whether these probes can be of diagnostic value in conjunctival melanomas.

The 4 probes that will be used are: RREB1, MYB, CCND1 and centromere 6. In this study

the test will be performed on excised specimens of conjunctival melanocytic lesions. Based on some well-defined cut-off criteria, the result of the FISH will be either positive or negative. In cutaneous melanomas this test proved to be very accurate in determining whether the lesions are benign or malignant. In this study the relevance of this simple test in conjunctival melanocytic lesions will be studied.

All molecular pathologic data will be correlated with the clinical, histological and immunohistochemical data available for these tumours. In so doing we will try to partly unravel the first bits of the molecular profile of ocular melanocytic lesions.

MAJOR REFERENCES:

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