Abstract

Over the last few years there has been growing interest in the study of genes involved in DNA repair, maintenance of genomic integrity, control of cell proliferation and differentiation, or in the metabolism of carcinogenic compounds.

Cyclin D1 gene (CCND1) is a proto-oncogene involved in cell cycle regulation, particularly important for the G1/S checkpoint of the cell cycle. This gene is altered in several kinds of tumors. The importance of cyclin D1 expression has been demonstrated in several studies. Iron (Fe) has an important role in cell cycle and tumorigenesis, with iron depletion leading to cell cycle arrest, stopping G1/S progression, and consequently leading to apoptosis.

Recent work demonstrates that cyclin D1 is over-expressed in the iron overloaded liver, and that the expression of cyclin D1 is induced by iron, and can contribute to cell cycle abnormalities. It was also demonstrated that cyclin D1 is expressed in peripheral blood lymphocytes.

The work presented in this thesis describes the analysis of Cyclin D1 expression (CCND1) in peripheral blood lymphocytes, and evaluates its correlation with iron overload in vivo. To accomplish that goal the expression of Cyclin D1 (CCND1) was analyzed in patients that suffer from Hereditary Hemochromatosis (HH), an autossomic recessive disease with altered iron metabolism, and which is characterized by increased iron absorption.

Two groups of patients were analyzed for CCND1 expression, one undergoing intensive treatment, and the other under maintenance treatment; healthy individuals formed the control group. This study was performed with peripheral blood samples collected from Hemochromatosis patients that undergo regular phlebotomy at the “Serviço de Hematologia Clínica do Hospital Geral de Santo António”, and controls were obtained from healthy blood donors that use the same unit. This study included fifty eight (58) individuals, of which thirty five (35) were men, and twenty three (23) women. Fifty (50) samples were from Hereditary Hemochromatosis patients, of which thirteen (13) were under intensive treatment and thirty seven (37) were in maintenance treatment. The
remaining eight (8) individuals were healthy blood donors, and constitute the control group.

The quantification of cyclin D1 expression was performed by *Real-Time Polymerase Chain Reaction* (RT-PCR).

The data analysis showed no overall differences between patients and controls. However, when analyzing the patients group in more detail, the results show that those undergoing intensive treatment have higher cyclin D1 expression, when compared to the ones on maintenance treatment. The results obtained also demonstrate the presence of cyclin D1 in lymphocytes, as all the samples studied showed relative cyclin D1 expression. The implications of these results are discussed.