Absence of rearrangements or activating mutations in the in the RTK III and IV family genes in BCR-ABL1 negative and JAK2V617F negative chronic myeloproliferative neoplasms (CMPNs)

Paula Aranaz, Cristina Ormazábal, Cristina Hurtado, Ignacio Erquiaga, Maria J. Calasanz, Marina García-Delgado, Francisco J. Novo, José L. Vizmanos

Department of Genetics, School of Sciences, University of Navarra, Pamplona, Spain

Keywords: Myeloproliferative neoplasms, tyrosine kinases

Abstract

BCR-ABL1 negative chronic myeloproliferative neoplasms (CMPNs) are a heterogeneous group of clonal haematological malignancies. Over the last years, some genetic alterations have been described to cause these diseases, most of them activating tyrosine kinase (TK) genes. Tyrosine kinases (TK) have an important role in cell growth and oncogenesis, as gain-of-function mutations can lead to the constitutive activation of the signalling pathways in which they are involved. In this study, we have analysed all genes from the families III (PDGFRA, PDGFRB, CSF1R, KIT and FLT3) and IV (FGFR1, FGFR2, FGFR3 and FGFR4) of RTKs. All of them code for receptors with tyrosine kinase activity and some of them have been found mutated in CMPNs and in other tumor types. We have used FISH to detect cryptic rearrangements and dHPLC to detect sequence mutations on samples from 44 BCR-ABL1 negative and V617FJAK2 negative CMPN patients. Both analyses have shown that these genes are no frequently mutated in these diseases, implying that molecular events or cryptic rearrangements causing these diseases, if they exist, must be located in other genes.