Research Project Proposal
Academic year 2018-2019

Project Nº 49

Title: *Challenges in the detection of clinically-relevant mutations in ABL1 gene in patients with Chronic Myeloid Leukemia. Evolution of technology, needs and new solutions.*

Department/ Laboratory *Hematological Diseases Lab, CIMA LAB Diagnostics, Lab. 1.04, CIMA*

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Summary

Patients with chronic myeloid leukemia (CML) receive Tyrosine kinase inhibitors (TKIs) targeting the BCR-ABL1 oncoprotein as the standard therapy.. However, a fraction of patients receiving first-line imatinib therapy will eventually require an alternative treatment because of intolerance or resistance to TKIs. The best-characterized mechanism of resistance is point mutations within the *BCR-ABL1* kinase domain that impair or prevent TKI binding. The detection of those mutations is therefore critical for the pharmacological management of CML patients. Sanger sequencing is the method most widely used for mutation detection, but it frequently fails to detect minor resisting clones emerging during TKI treatment. It is therefore compelling to explore alternative and more accurate methods able to detect such minor clones.

Next-Generation Sequencing (NGS) has emerged as a promissing technique to revolutionize nucleic acid sequencing, and numerous publications have proved its clinical utility. However, the variability of BCR-ABL1 breakpoints makes it difficult to desing an NGS tool able to address the molecular follow-up of CML patients. This compelling clinical need requires careful testing of new NGS tools before implementing them in the clinical routine.

The Master Student will test an NGS tool developed by CIMA LAB Dx, using Archer Dx technology, and will compare it with the gold-standard techniques currently used in the clinical setting (qPCR and Sanger sequencing). The Student will determine the ability of this tool to quantify known transcripts, detect minor mutant clones, and monitor the potential aparition of emerging new BCR-ABL1 transcripts in a cohort of CML patients under TKI treatment.

yes	
no	**X**

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?