

## **CD38<sup>+</sup> sub-populations have increased proliferative activity but similar telomere lengths and *hTERT* expression when compared with CD38<sup>-</sup> sub-populations derived from the same CLL patient**

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CD38 expression is as an important poor prognosis marker in B-cell chronic lymphocytic leukemia (B-CLL) but the biological rationale for this remains obscure. We have recently shown that CD38<sup>+</sup> sub-populations have an increased proliferative activity when compared with their CD38<sup>-</sup> counter-parts, as evidenced by higher Ki-67 expression (n=20; P<0.0001). This finding raised the possibility that the CD38<sup>+</sup> fraction of the individual patients may have different proliferative histories and are exposed to a disproportionate risk of clonal evolution through the acquisition of secondary cytogenetic lesions.

Therefore, we determined the proliferative histories by measuring telomere length, telomerase activity and telomerase (*hTERT*) expressions in CD38<sup>+</sup> and CD38<sup>-</sup> sub-populations derived from the peripheral blood of 20 CD38 bimodal patients. Telomere length analysis revealed that all of the sub-populations had similarly short telomeres (P=0.31) and comparable (low) telomerase (*hTERT*) expression (P=0.75) and telomerase activity. Furthermore, FISH analysis revealed that the CD38<sup>+</sup> sub-populations had no distinct cytogenetic lesions or evidence of clonal evolution when compared with their CD38<sup>-</sup> counter-parts derived from the same bimodal B-CLL patients (n=37).

In addition, subsequent examination of paired peripheral blood and bone marrow samples revealed no significant difference in CD38, Ki-67, *hTERT* expression or telomere lengths indicating that these B-CLL cells were derived from a single pool constantly trafficking between these two compartments. Taken together, our data suggest a model of CD38 plasticity in bimodal patients in which all of the clones periodically express CD38 and undergo proliferation.