LymphomaHub

BL

AACR 2017 | Poster 2447/4 – The mutational landscape of chemo-refractory Burkitt Lymphoma

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On Monday 3rd April during this year's American Association for Cancer Research (AACR) annual meeting, a poster (2447 / 4) by Claudia M. Wever, from McGill University, Montreal, QC, Canada, *et al.* titled "The mutational landscape of chemo-refractory Burkitt lymphoma" was presented.

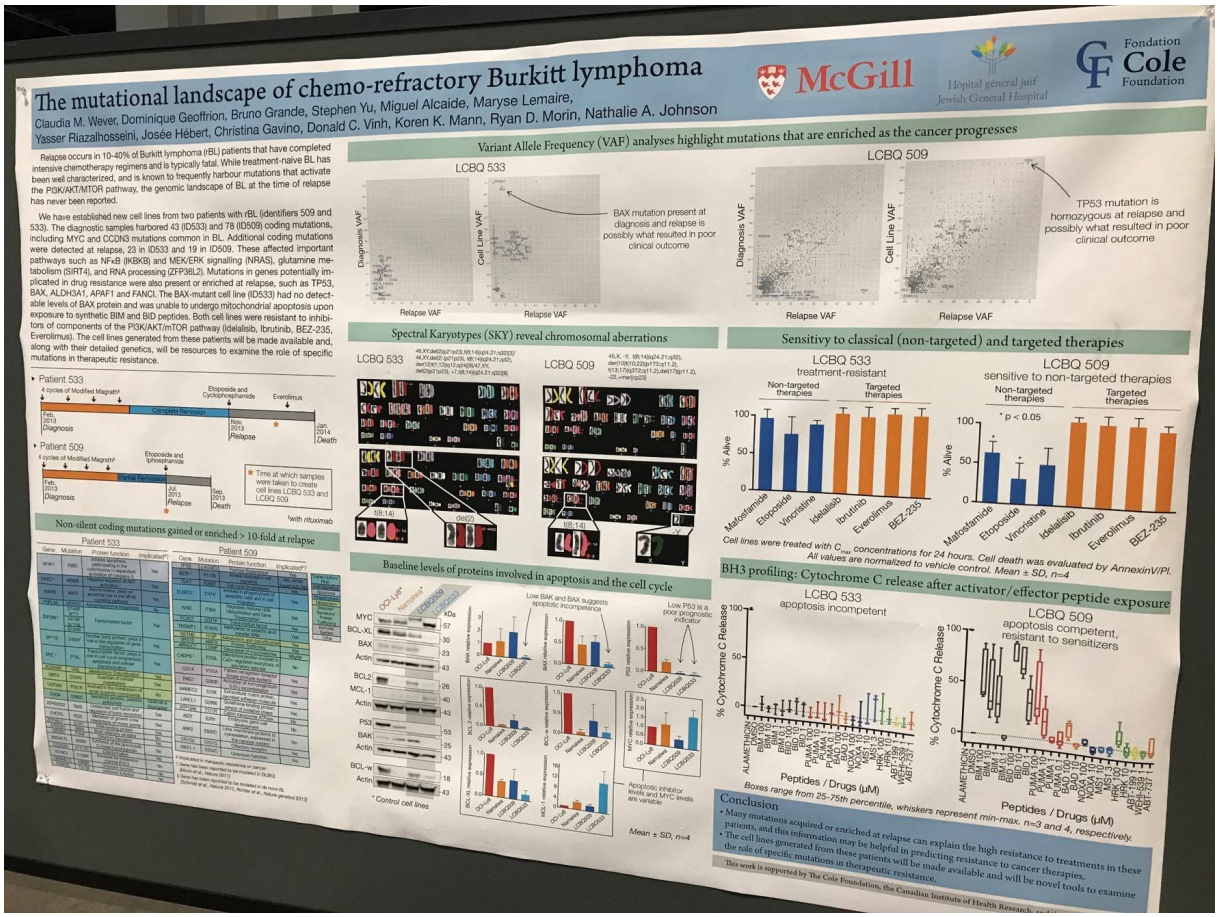
Burkitt Lymphoma (BL) is rarely re-biopsied at time of relapse, and so the mutational landscape of relapsed BL is very ill defined. Two, young, male patients experienced relapse after completion of intensive chemotherapy within 3 months. The group aimed to identify mutations which may have contributed to therapy resistance as well as to create cell lines from the two patients in order to study the tumors in more detail.

Tumor cells from the two patients underwent whole exome sequencing at time of diagnosis (T1) and relapse (T2); unaffected peripheral blood was used to exclude germline variants. Samples from T2 were used to create the novel cell lines (CLs) which were sequenced and karyotyped.

Key Highlights:

- Total number of coding mutations:
  - In first patient: T1 = 78, T2 = 84, CL= 63
  - In second patient: T1= 43, T2 = 66, CL= 70
- All samples had multiple missense mutations (5–7) in MYC and had evidence of clonal heterogeneity
- First patient:
  - Harbored a TP53 (R248) mutation that was clearly selected for during chemotherapy, where the variant allele fraction increased from 2–93% between T1 and T2
  - Missense mutations were acquired by 19 genes at T2 including: CD14, GSTM3, BCR, and ELMO3
  - In CL, several genomic rearrangements were reported by karyotyping: Y,t(8;14)(q24.21;q32), del(10)t(10;22)(p1?3;q11.2), t(13;17)(q3?2;q11.2), del(17)(p11.2), and -22
- Second patient:
  - Multiple frameshift mutations present in T1, T2, and CL; found in CCND3, BAX, ARID1A, ARID1B, DDX5, DETD1B, TSFM, SP3, and TFAP4
  - T2 and CL had additional acquired missense or nonsense mutations in ZFP36L2, CCL7, FAM13C, and IKBKB
  - CL had 3 dominant clones by karyotype
  - In CL, the rearrangements observed were: del(2)(p21p23), t(8;14)(q24.21;q32), t(1;12)(q12;q24), and +7
  - The frameshift mutations in ZFP36L2 and BAX were homozygous in CL

The group stated that, to their knowledge, “these are the first BL cell lines that have been well-characterized with respect to the serial acquisition of mutations after exposure to chemotherapy and with knowledge of germline variants.” The poster concluded by stating that their CLs are a useful tool which will enable oncogene co-operation, clonal evolution, chromatin remodeling, RNA processing, and apoptosis to be studied in BL.



Reference:

1. Wever C.M. *et al.* The mutational landscape of chemo-refractory Burkitt lymphoma [Poster]. In: Proceedings of the 107th Annual Meeting of the American Association for Cancer Research; 2017 Apr 1-5; Washington, DC. Philadelphia (PA): AACR; 2017. Poster nr [2447 / 4].