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| cLINICAL UTILITY OF MOLECULAR TESTING IN  LOW GRADE b-CELL LYMPHOMAS  DIAGNOSTIC utility  *MYD88* Leu265Pro mutations are observed in >90% of Waldenstrom macroglobulinaemia/lymphoplasmacytic lymphoma (WM/LPL)1,2, the majority of IgM-MGUS3, 5-10% of marginal zone lymphoma (MZL)1,4 and <5% of chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL)5. *MYD88* mutations are not observed in plasma cell myeloma (PCM)1.  Non-canonical *MYD88* mutations have been observed in rare cases of WM/LPL3.  *CXCR4* mutations are seen in approximately 30% of WM/LPL and 5-10% of IgM-MGUS3,6,7. Mutations in *CXCR4* almost always coexist with the *MYD88* L265P mutation (98% of cases)7. *CXCR4* mutations are uncommon in other low grade B-cell lymphomas including CLL/SLL8, except for follicular lymphoma (FL) where they may be observed without *MYD88* mutations9.  Other genes that are recurrently mutated in WM/LPL include *CD79B* and *TP53*3,7.  A number of mutations are observed in CLL/SLL including *NOTCH1, BIRC3, SF3B1, MYD88, XPO1, ATM*, MAPK pathway genes (*BRAF, NRAS, KRAS, MAP2K1*) and *TP53*10,11. These are not specific for a diagnosis of CLL/SLL except for *SF3B1* mutations which are not commonly observed in other B cell malignancies12.  Mantle cell lymphoma (MCL) is genetically characterised by t(11;14) (best detected by FISH). Recurrently mutated genes in MCL include *ATM, KMT2D, TP53, CCND1, WHSC1, BIRC3* and *NOTCH1/NOTCH2*13-15.  Somatic mutations recurrently observed in MZL (both nodal and splenic) include *KLF2* (relatively specific for MZL diagnosis), *NOTCH2, KMT2D* and *TP53*16,17. Mutations in epigenetic modifiers (e.g activating *EZH2* mutations, *TET2, CREBBP*) are more commonly observed in nodal MZL compared to splenic MZL18.  Genes commonly mutated in FL include *KMT2D, CREBBP, EZH2* (activating mutations), *ARID1A* and *EP300*19-21.  The defining genomic lesion in classic hairy cell leukaemia (HCL) is the somatic *BRAF* Val600Glu mutation, which is present in almost all cases22.  Whilst *BRAF* Val600Glu mutations are typically absent in morphologic mimics of HCL including hairy cell leukaemia variant (HCL-v), splenic MZL and splenic diffuse red pulp small B-cell lymphoma (SDRPL)22-24, they may be observed in CLL/SLL, PCM, nodal MZL and histiocytic malignancies18,25-27.  PROGNOSTIC utility  *TP53* mutations are associated with inferior outcomes across the spectrum of low grade B-cell lymphomas including CLL28-30, MCL15, WM/LPL31 and MZL17.  In WM/LPL, *MYD88* mutations are associated with more favourable outcomes while *CXCR4* mutations are associated with more aggressive disease6,32.  BIOMARKERS OF RESPONSE TO THERAPY  In WM/LPL, *CXCR4* mutations are associated with an inferior response to single agent ibrutinib33,34.  Acquired resistance to ibrutinib in WM/LPL has been associated with recurrent mutations involving the ibrutinib binding site of *BTK* (most commonly *BTK* Cys481)35.  In HCL the *BRAF* Val600Glu mutation is the target of BRAF inhibitors36. Additionally, activating MAPK pathway mutations (*BRAF, NRAS, KRAS, MAP2K1*) represent a potential target of MEK inhibition37.  REFERENCES  **1.** Treon SP, et al. MYD88 L265P somatic mutation in Waldenstrom's macroglobulinemia. *N Engl J Med* 2012; **367**(9): 826-33. **2.** Poulain S, et al. MYD88 L265P mutation in Waldenstrom macroglobulinemia. *Blood* 2013; **121**(22): 4504-11. **3.** Varettoni M, et al. Pattern of somatic mutations in patients with Waldenström macroglobulinemia or IgM monoclonal gammopathy of undetermined significance. *Haematologica* 2017; **102**(12): 2077-85. **4.** Ngo VN, et al. Oncogenically active MYD88 mutations in human lymphoma. *Nature* 2011; **470**(7332): 115-9. **5.** Puente XS, et al. 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