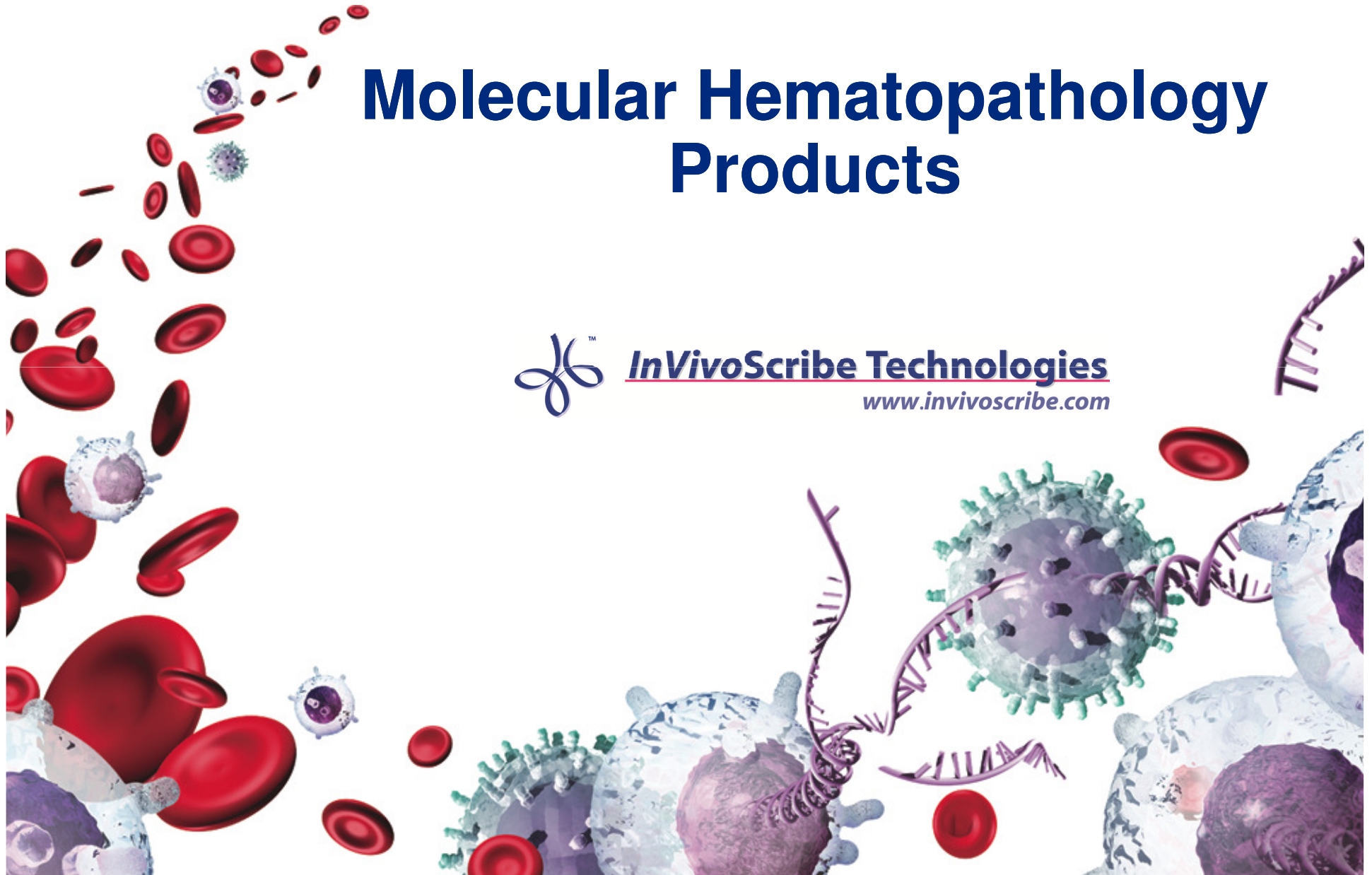


Molecular Hematopathology Products



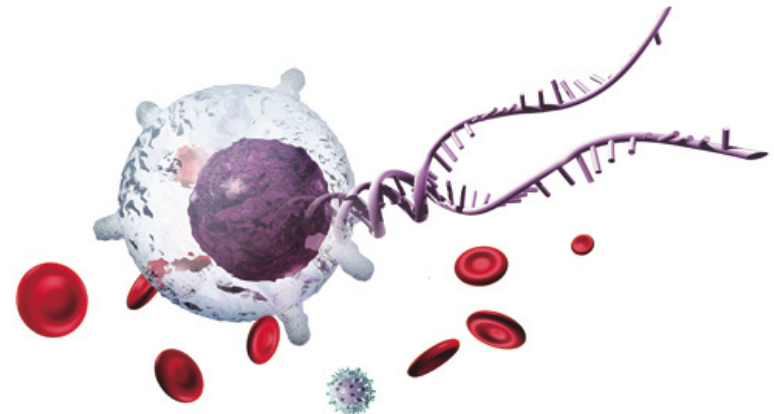
InVivoScribe Technologies

www.invivoscribe.com



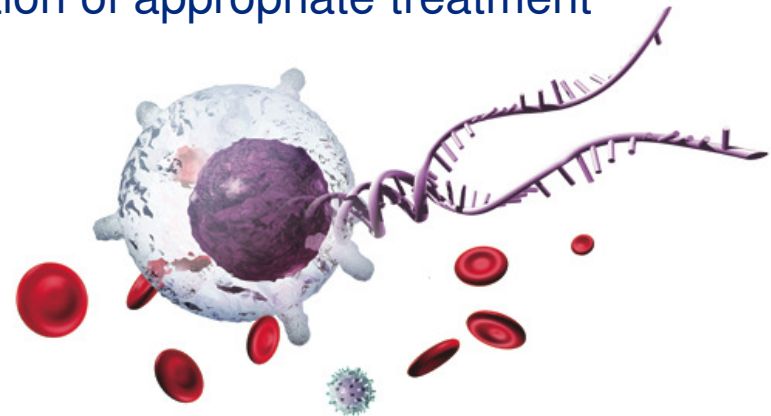
InVivoScribe Technologies

- Provides a comprehensive selection of PCR-based molecular hematopathology testing reagents and controls
 - Assays used in over 40 countries worldwide



PCR-based Molecular Hematopathology Testing Reagents and Controls

- Efficient and reliable standardized tests, reagents, and controls
 - Detection of clonal rearrangements and genetic abnormalities associated with hematologic disease
- Extensive validation, quality control, and quality assurance
 - Products that streamline molecular diagnostic laboratory throughput
 - Ensures consistent product and laboratory results
- Cutting-edge tools used for improving the quality of healthcare
 - Rapid turnaround of analysis
 - Essential diagnostic tools used for selection of appropriate treatment strategy



InVivoScribe Products

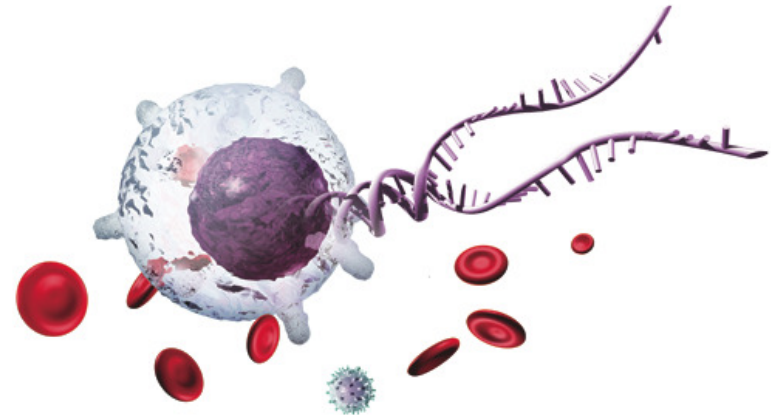
- Products for Molecular Hematopathology Testing

- Assays for detection of:

- Clonal gene rearrangement
 - Chromosome translocations
 - Gene mutations

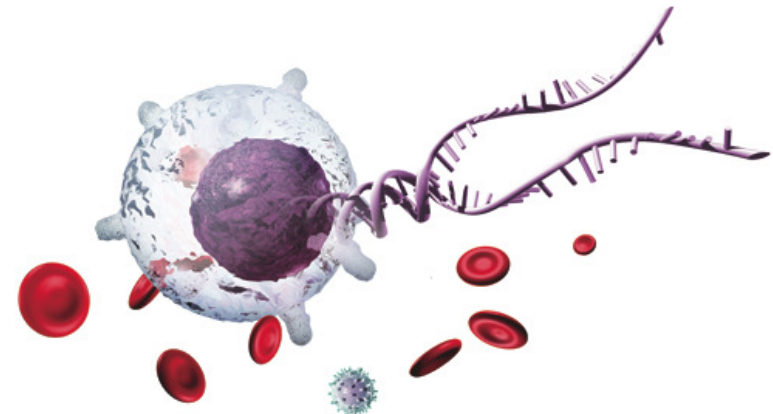
- Reference standards and controls:

- DNA: locus/target, sensitivity panels, polyclonal, tonsil tissue, cell lines, plasmid
 - RNA: locus/target, sensitivity panels, proficiency panels, cell lines



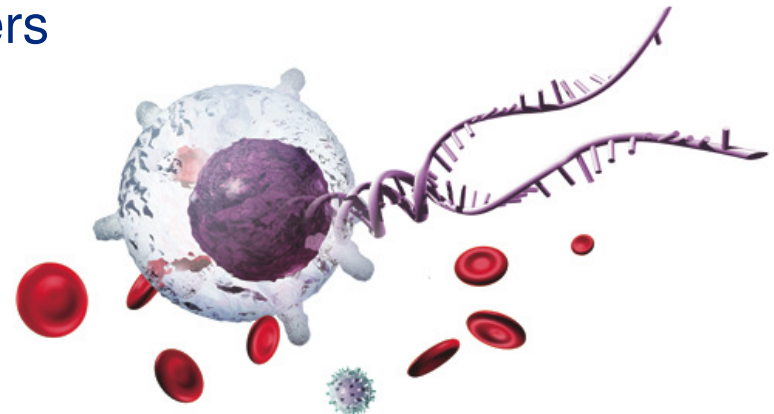
InVivoScribe Products

- Products for Molecular Hematopathology Testing
 - Master Mixes: components of assay kits
 - Target specified locus
 - Template amplification controls
 - Reagents:
 - PCR/cDNA (buffer, MgCl₂, dNTP mix)
 - Gel detection
 - ABI fluorescence detection



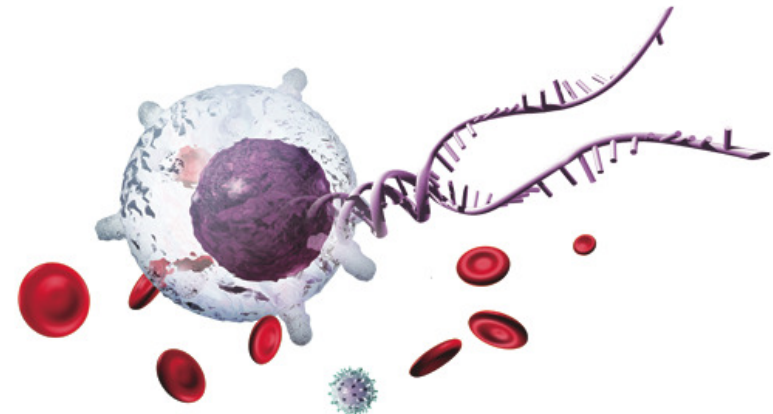
Background of Clonal Ig and TCR Gene Rearrangements

- Immunoglobulin and TCR Gene Rearrangements:
 - Stepwise rearrangement process, during lymphocytic cell maturation, creates unique antigen-receptor genes
 - Random DNA bases are inserted during the rearrangement process causing diversity in the length of antigen-receptor genes
 - PCR amplification identifies the varying gene lengths resulting from random base insertion
 - PCR-based assays allow for the identification of clonality in atypical lymphoproliferative disorders



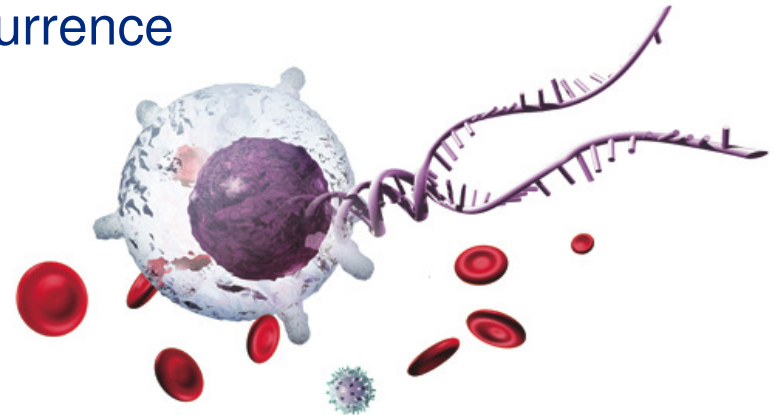
Ig Gene Rearrangement Assays

- Ig Gene Rearrangement/Clonality Assay Uses:
 - Identify clonality in atypical lymphoproliferative disorders
 - Discriminate between reactive lesions and hematologic malignancy
 - Assign presumptive lineage in mature monoclonal lymphoproliferative disorders
 - Identify tumor-specific markers for post-treatment monitoring
 - Monitor and evaluate disease recurrence



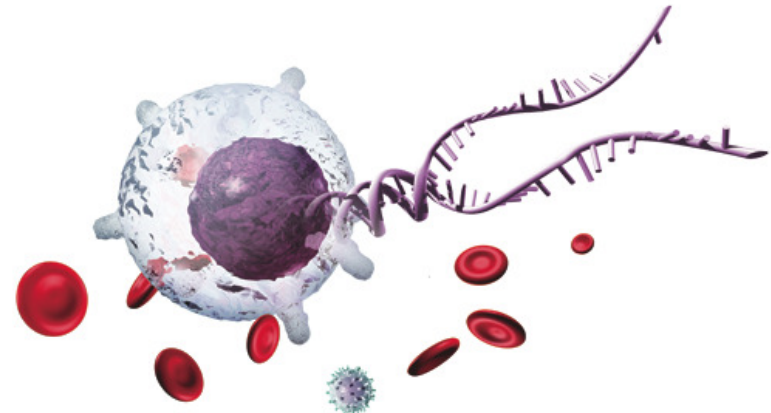
TCR Gene Rearrangement Assays

- TCR Gene Rearrangement/Clonality Assay Uses:
 - Identify clonality highly suggestive of T-cell and some immature B-cell malignancies
 - Discriminate between reactive lesions and hematologic malignancy
 - Determine lineage involvement in mature lymphoproliferative disorders
 - Identify tumor-specific markers for post-treatment monitoring
 - Monitor and evaluate disease recurrence



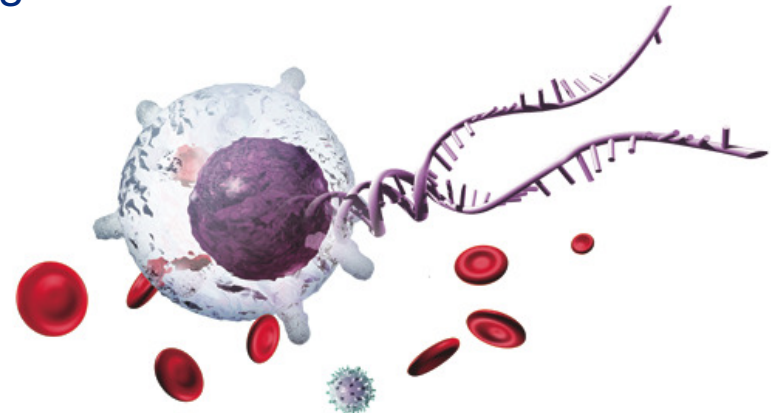
Clonal Gene Rearrangement Assays

- Immunoglobulin Gene Rearrangement/Clonality Assays:
 - IGH Gene Rearrangement Assays
 - 3 master mixes targeting the Framework 1-3 regions
 - IGH Gene Clonality Assays
 - 3 master mixes targeting the Framework 1-3 regions
 - 2 master mixes targeting the DH-JH rearrangements
 - BIOMED-2 Concerted Action Group



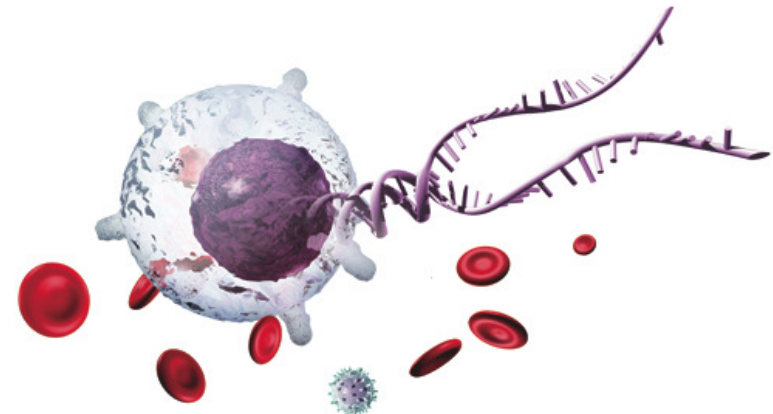
Clonal Gene Rearrangement Assays

- Immunoglobulin Gene Rearrangement/Clonality Assays:
 - IGK Gene Clonality Assays
 - 2 master mixes targeting the Vk1-7 segments, the Kappa deletion element, and intron segment
 - BIOMED-2 Concerted Action Group
 - IGL Gene Clonality Assays
 - 1 master mix targeting the V λ 1-3 segments
 - BIOMED-2 Concerted Action Group



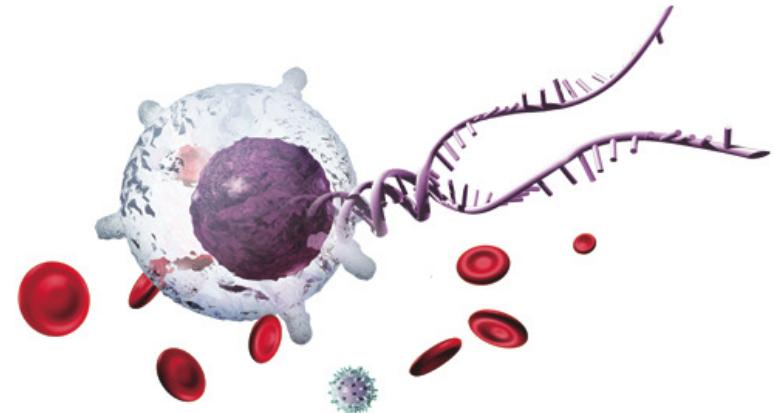
Clonal Gene Rearrangement Assays

- T Cell Receptor Gene Rearrangement/Clonality Assays:
 - TCRB Gene Clonality Assays
 - 3 master mixes targeting the Vb1-24 and Db1&2 gene segments
 - BIOMED-2 Concerted Action Group
 - TCRD Gene Clonality Assays
 - 1 master mix targeting the Vd1-6 and Dd2&3 gene segments
 - BIOMED-2 Concerted Action Group



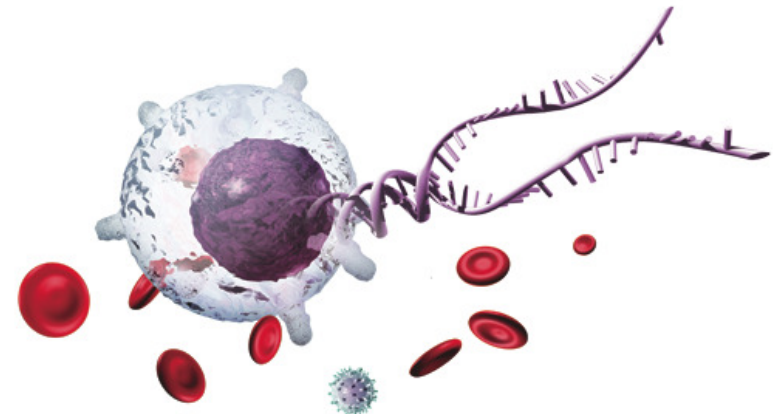
Clonal Gene Rearrangement Assays

- T Cell Receptor Gene Rearrangement/Clonality Assays:
 - T Cell Receptor Gamma Gene Rearrangement Assay
 - 2 master mixes targeting the Vg1-9 using 2 different primer binding sites
 - TCRG Gene Clonality Assays
 - 2 master mixes targeting the Vg1-11 gene segments
 - BIOMED-2 Concerted Action Group



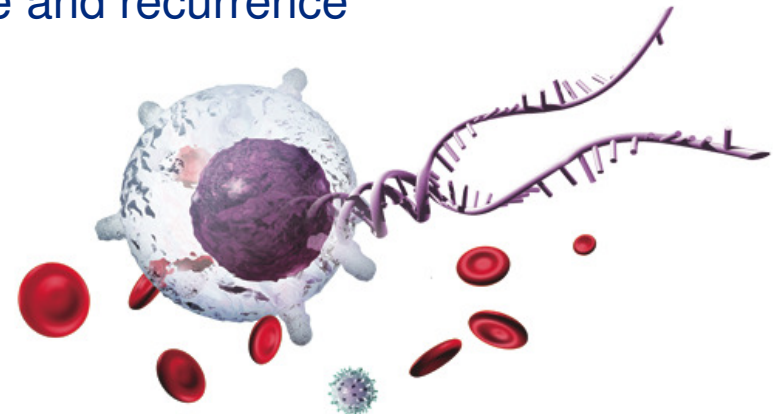
Clonal Gene Rearrangement Assays

- IGH Somatic Hypermutation Assay:
 - Determines extent of somatic hypermutation in the variable region of the immunoglobulin heavy chain gene in patients with chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL)
 - Presence of hypermutation is strongly predictive of a good prognosis



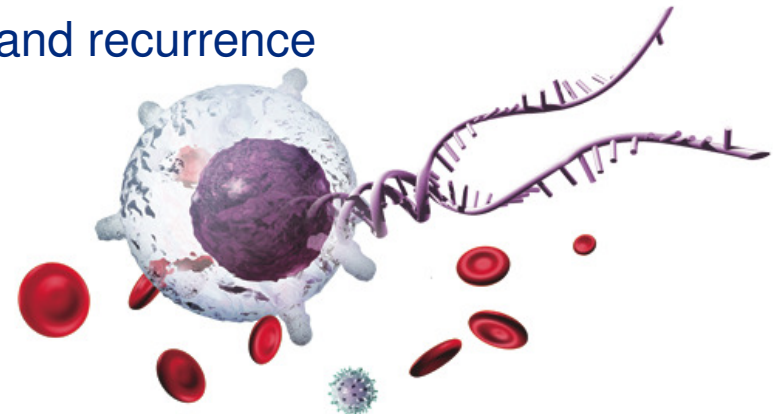
Chromosome Translocation Assays

- *BCL1/JH* t(11;14):
 - Highly suggestive of Mantle Cell Lymphoma (MCL)
 - Monitor and evaluate residual disease and recurrence
 - BIOMED-2 Concerted Action Group
- *BCL2/JH* t(14;18):
 - Distinguish lymphoma from benign lymphoid hyperplasia
 - Distinguish follicular lymphoma from other B-cell lymphomas having a similar appearance
 - Monitor and evaluate residual disease and recurrence



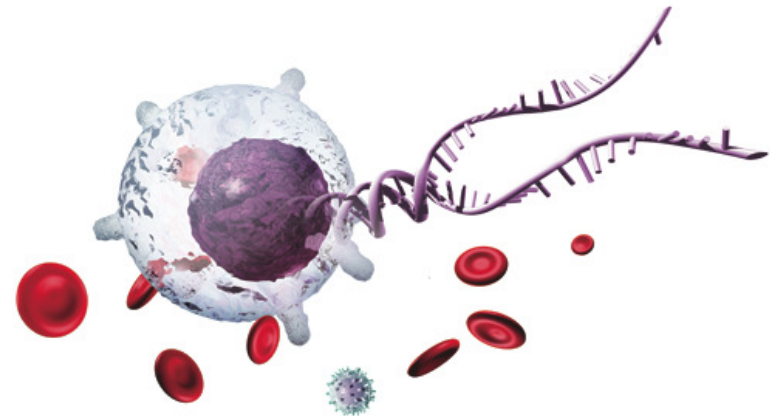
Chromosome Translocation Assays

- *BCL2/JH* Translocation Assay:
 - Distinguish lymphoma from benign lymphoid hyperplasia
 - Distinguish follicular lymphoma from other B-cell lymphomas having a similar appearance
 - Monitor and evaluate residual disease and recurrence
 - BIOMED-2 Concerted Action Group
- *BCR/ABL* t(9;22) Translocation Assay:
 - Identifies chronic myeloid leukemia (CML) and acute lymphoblastic leukemia (ALL)
 - Distinguish Ph⁺ ALL from lymphoid blast crisis
 - Monitor and evaluate residual disease and recurrence



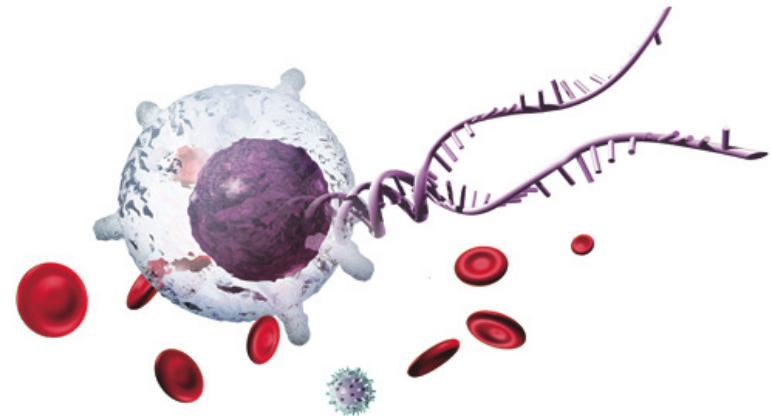
Chromosome Translocation Assays

- *PML/RAR α* t(15;17) Translocation Assay:
 - Identifies acute promyelocytic leukemia (APL)
 - Confirm presence of the *PML/RAR α* translocation prior to treatment with ATRA
 - Monitor and evaluate residual disease and recurrence



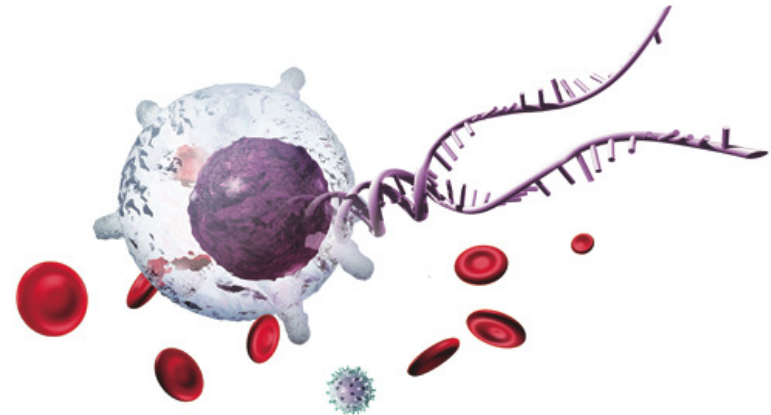
Mutation Assays

- *FLT3* Mutation Background:
 - Identifies *FLT3* mutations in patients with AML
 - Approximately 50% of AML patients have normal cytogenetic evaluations
 - *FLT3* is the single most important prognostic biomarker as it further characterizes patients with more aggressive disease
 - *FLT3* mutations can improve stratification of subgroups within AML



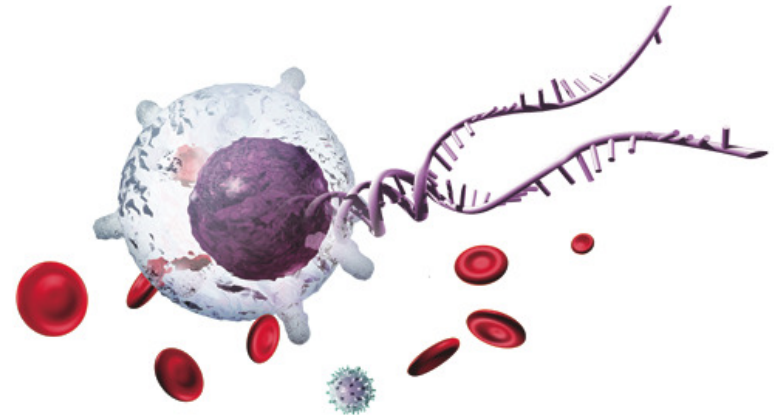
Mutation Assays

- *FLT3* Mutation Assay:
 - Identifies internal tandem duplications (ITD) of the juxtamembrane domain and tyrosine kinase domain (TKD) point mutations of the aspartic acid residue 835
 - *FLT3* ITD mutations portend a worse prognosis for AML patients
 - Patients testing positive for *FLT3* may be candidates for more aggressive therapy
 - IVS has exclusive license (worldwide, ex Japan) to patents covering testing for most prevalent and clinically relevant *FLT3* mutations



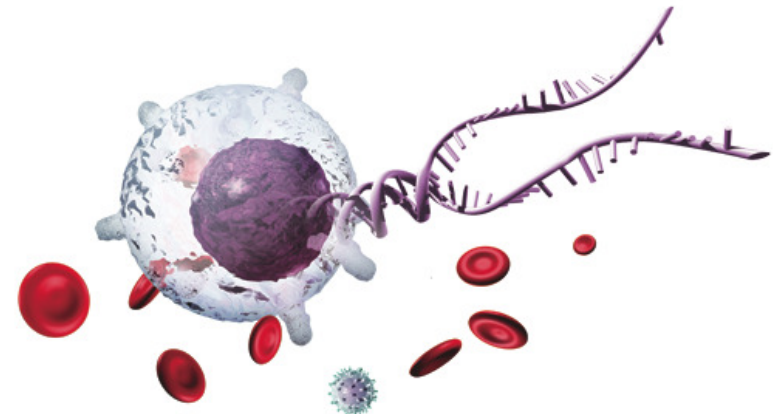
Assay Detection Options

- Assays and Master Mixes are available in several detection formats:
 - Gel detection: standard gel detection methods
 - ABI Fluorescence Detection: 6FAM, HEX, and NED fluorochromes
 - Beckman Coulter CE / NAT Platforms: D4, D3 and D2 flurochromes



Summary

- *InVivoScribe* Technology Products:
 - Efficient and reliable standardized tests, reagents, and controls
 - PCR-based detection for rapid turnaround of analysis
 - Extensive validation, quality control, and quality assurance
 - Designed for high-throughput and consistent results
 - Improving the quality of healthcare
 - Diagnostic tools for guiding personalized treatment strategies



Summary

- PCR-based products for molecular hematopathology diagnostics
 - Clonal Gene Rearrangement Assays: *InVivoScribe*/BIOMED-2
 - Chromosome Translocation Assays: *InVivoScribe*/BIOMED-2
 - Mutation Analysis: Exclusive license for *FLT3* testing
- Assays and Reagents available for detection on various platforms
 - Gel Detection
 - ABI Fluorescence Detection
 - Beckman Coulter CE / NAT Platforms

