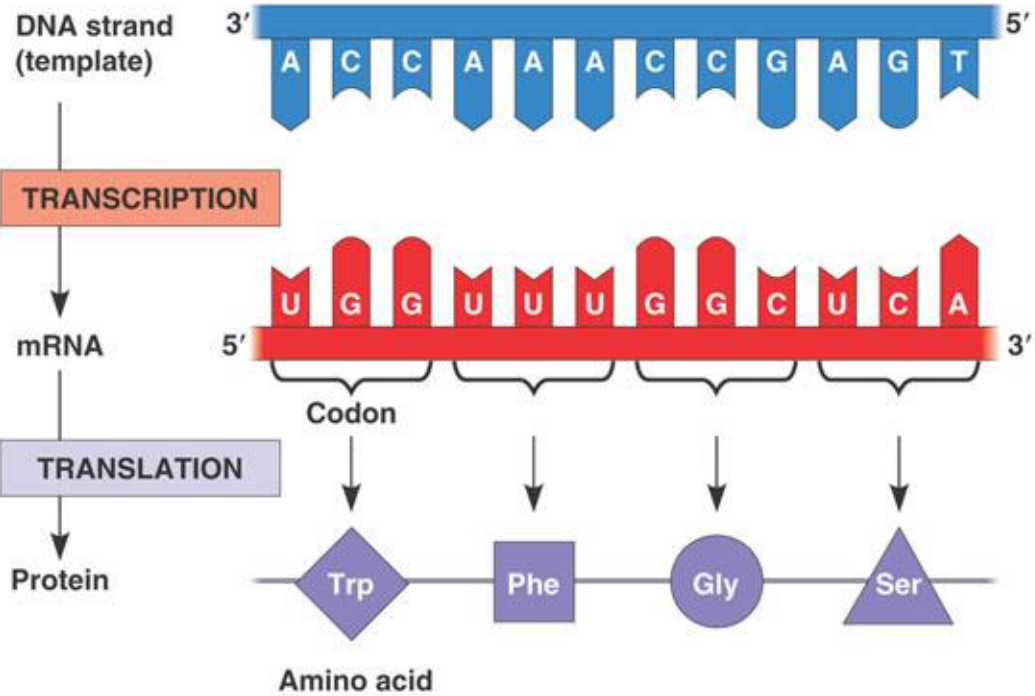
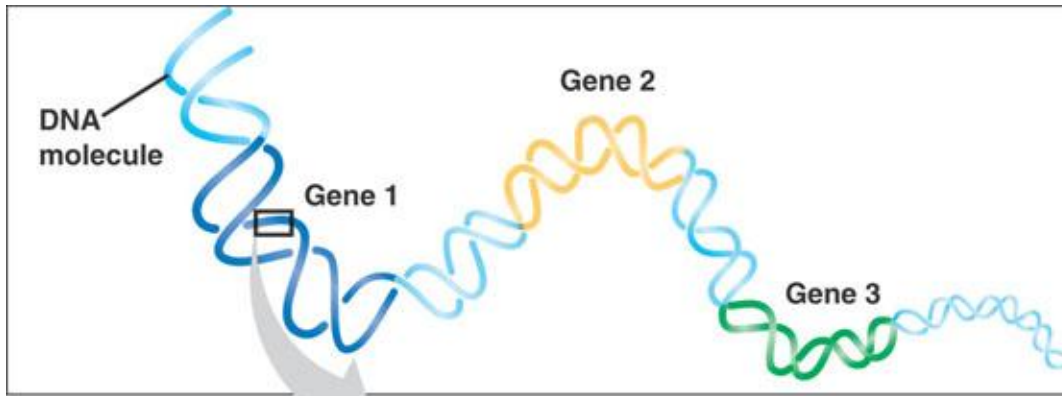


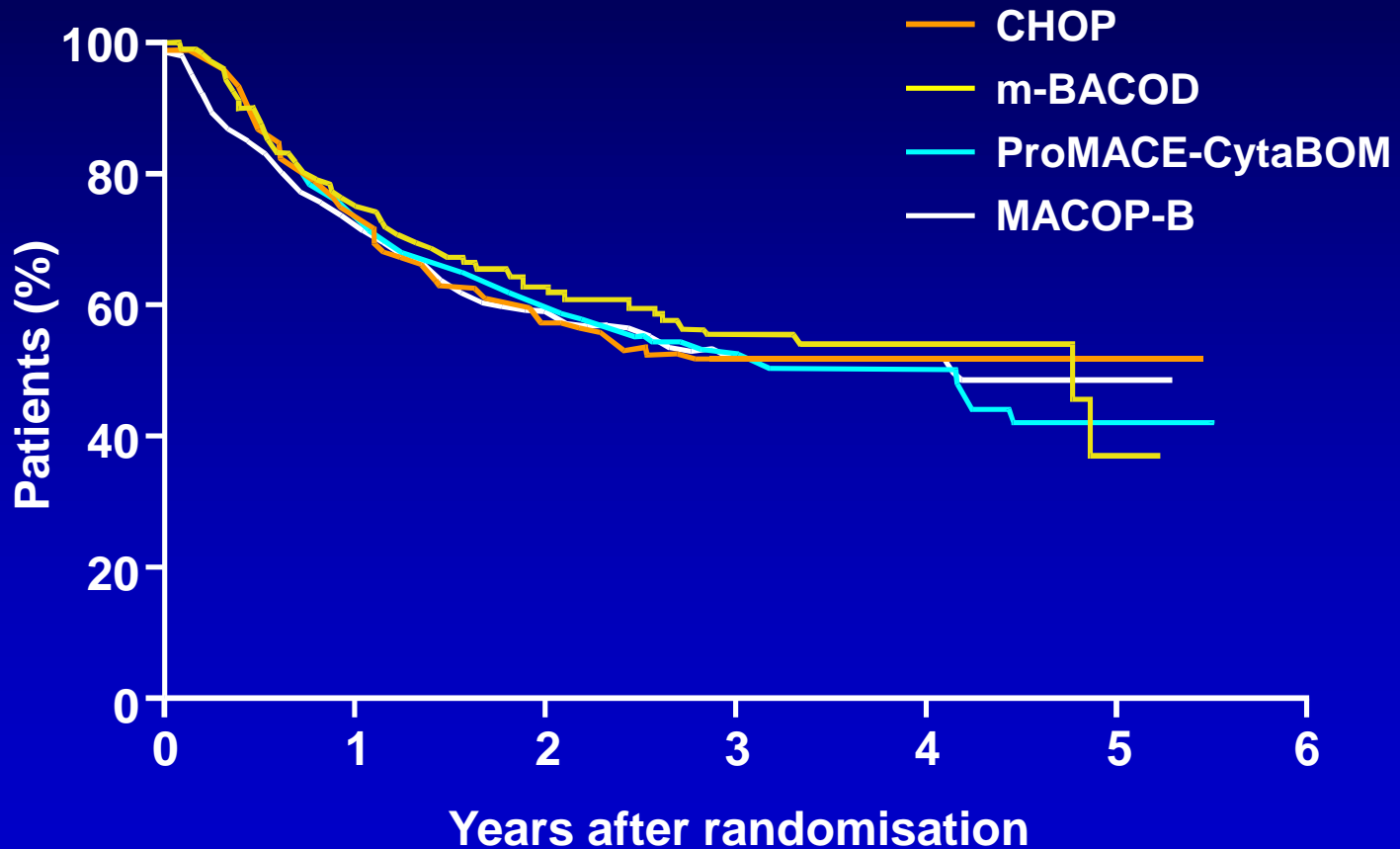
Le Lymphome et les Nouvelles Technologies Génomiques

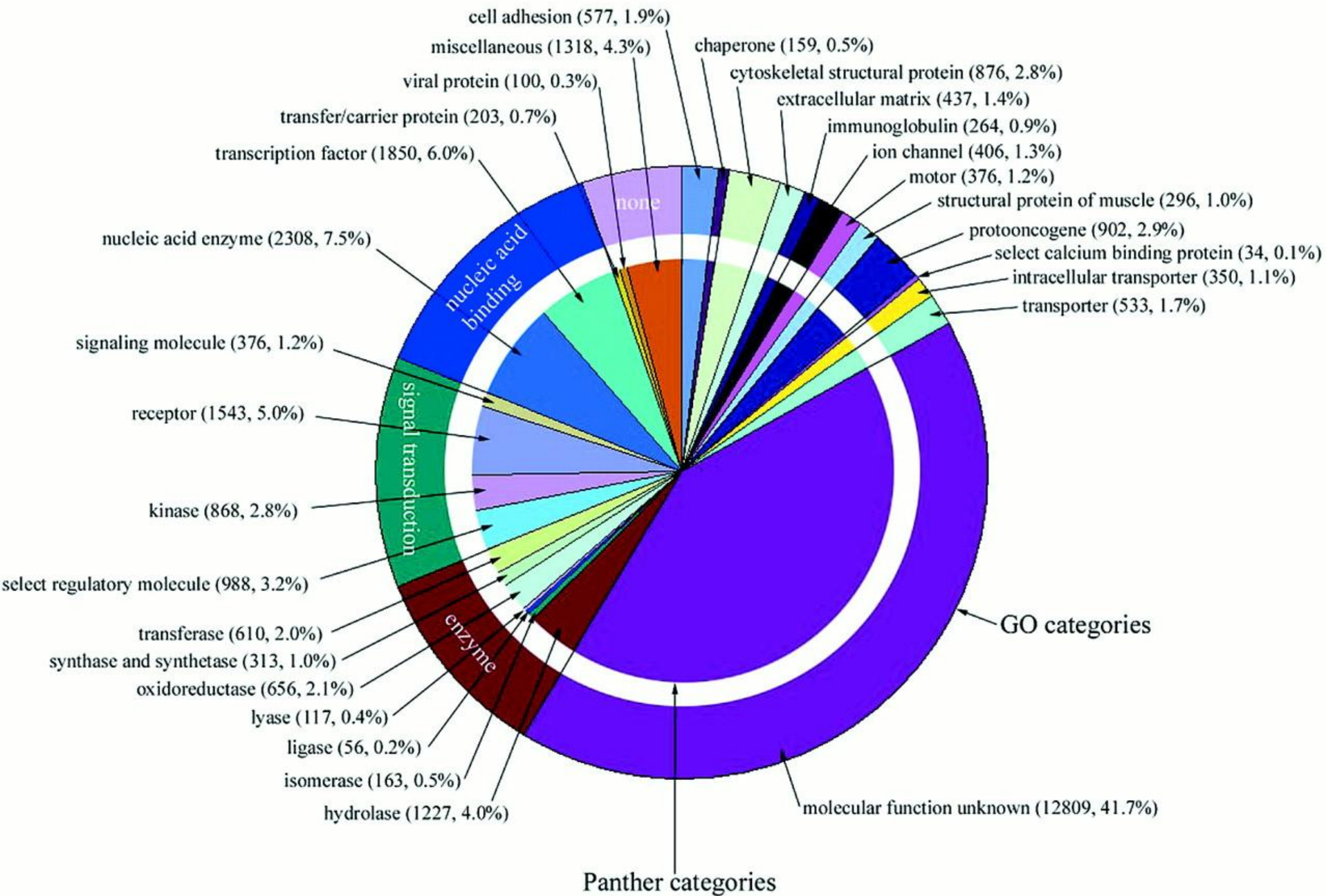
Pierre Laneuville, MD

Centre universitaire de santé McGill

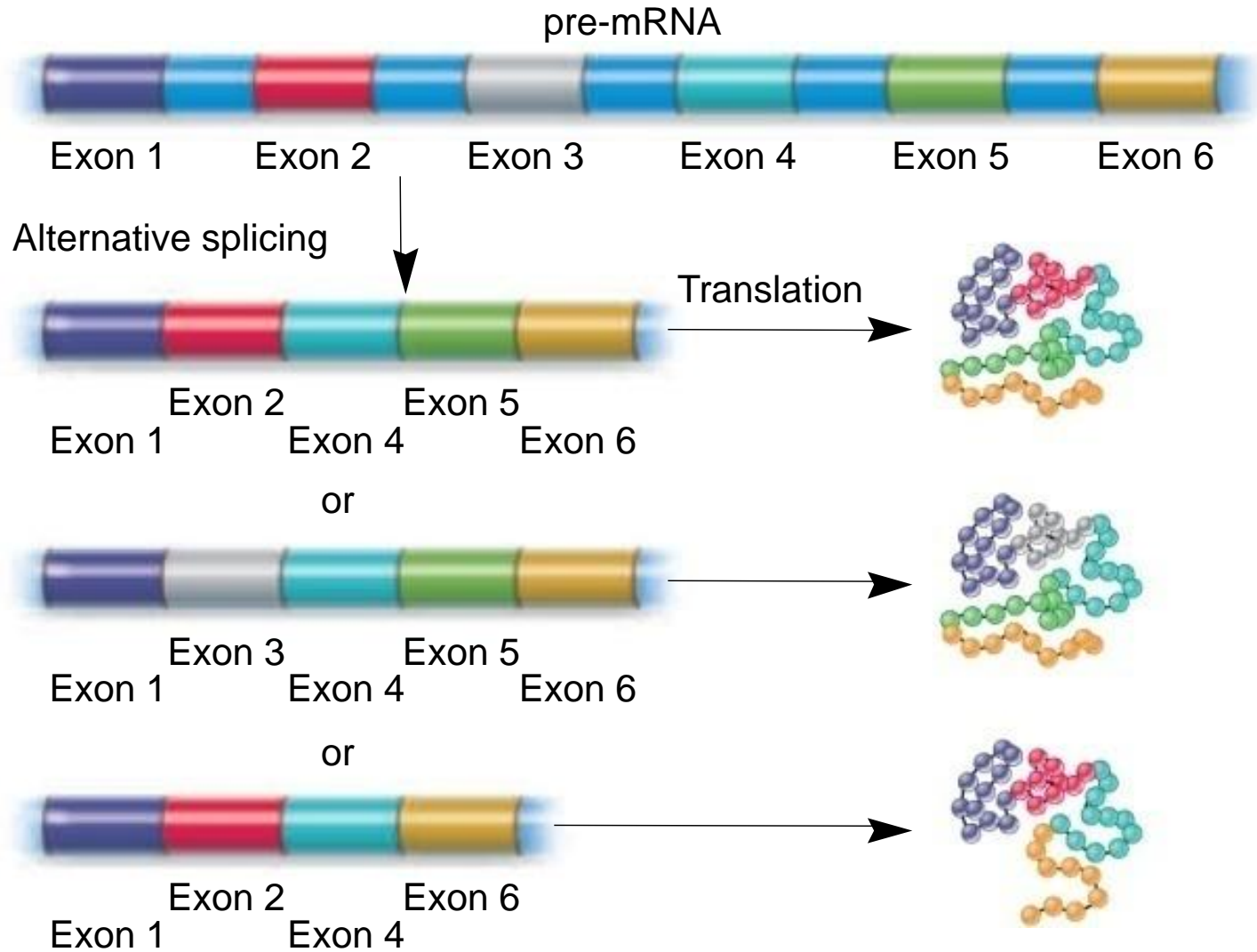


Progression-free survival in aggressive NHL: National High-Priority Lymphoma Study

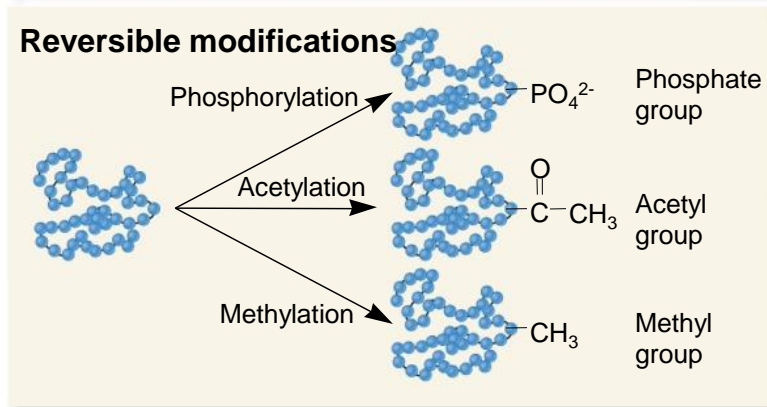
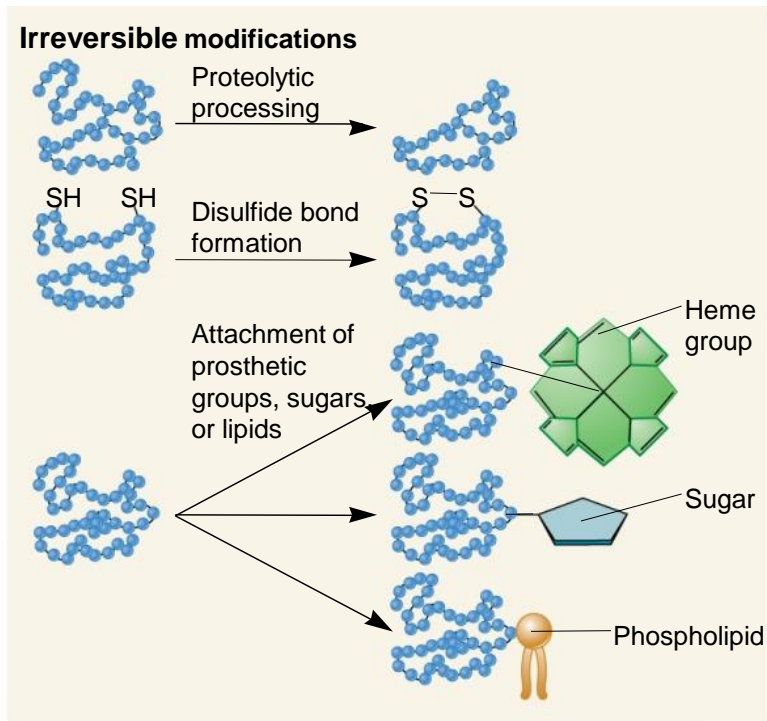




Why is the proteome so large? Alternative splicing



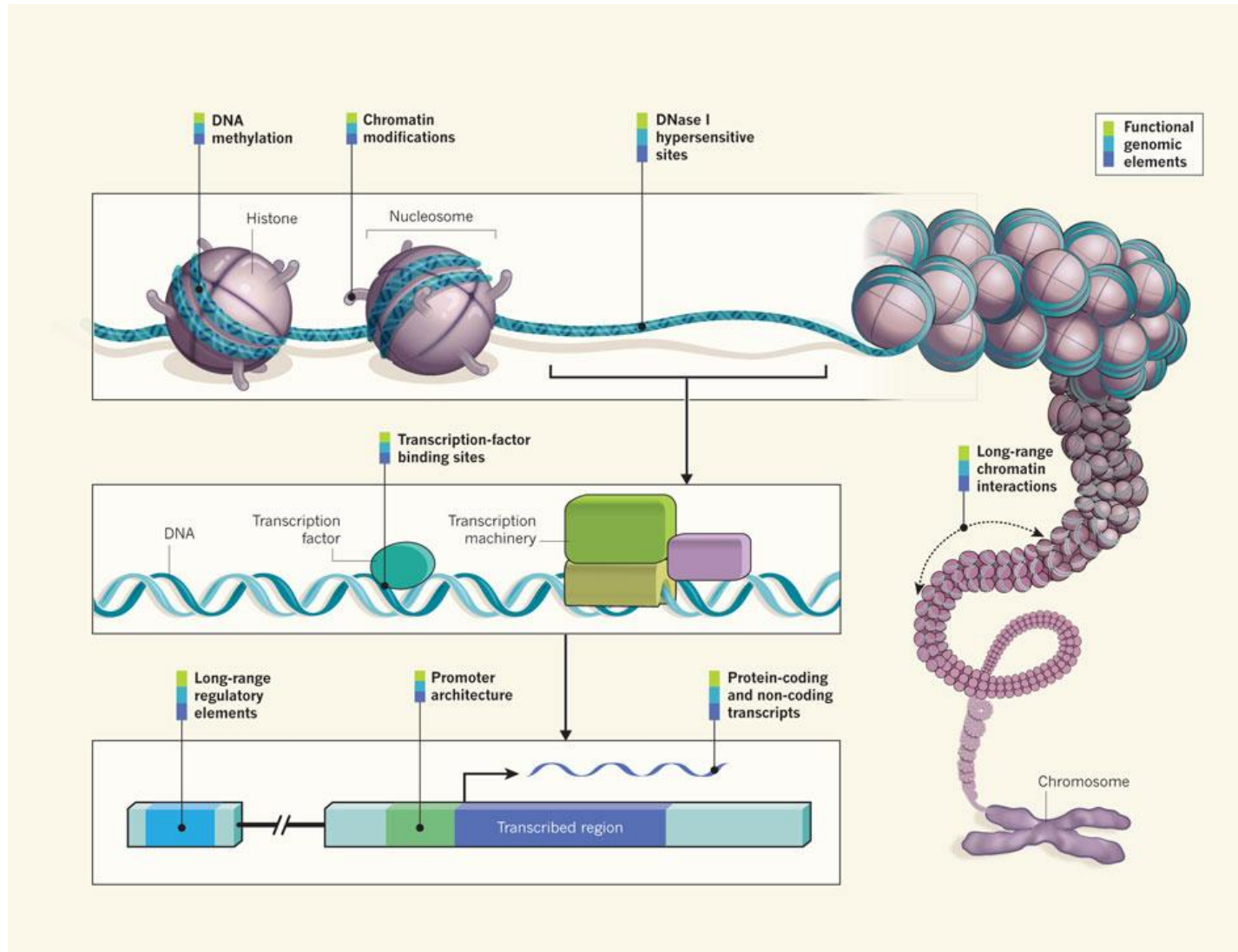
(a) Alternative splicing



(b) Posttranslational covalent modification

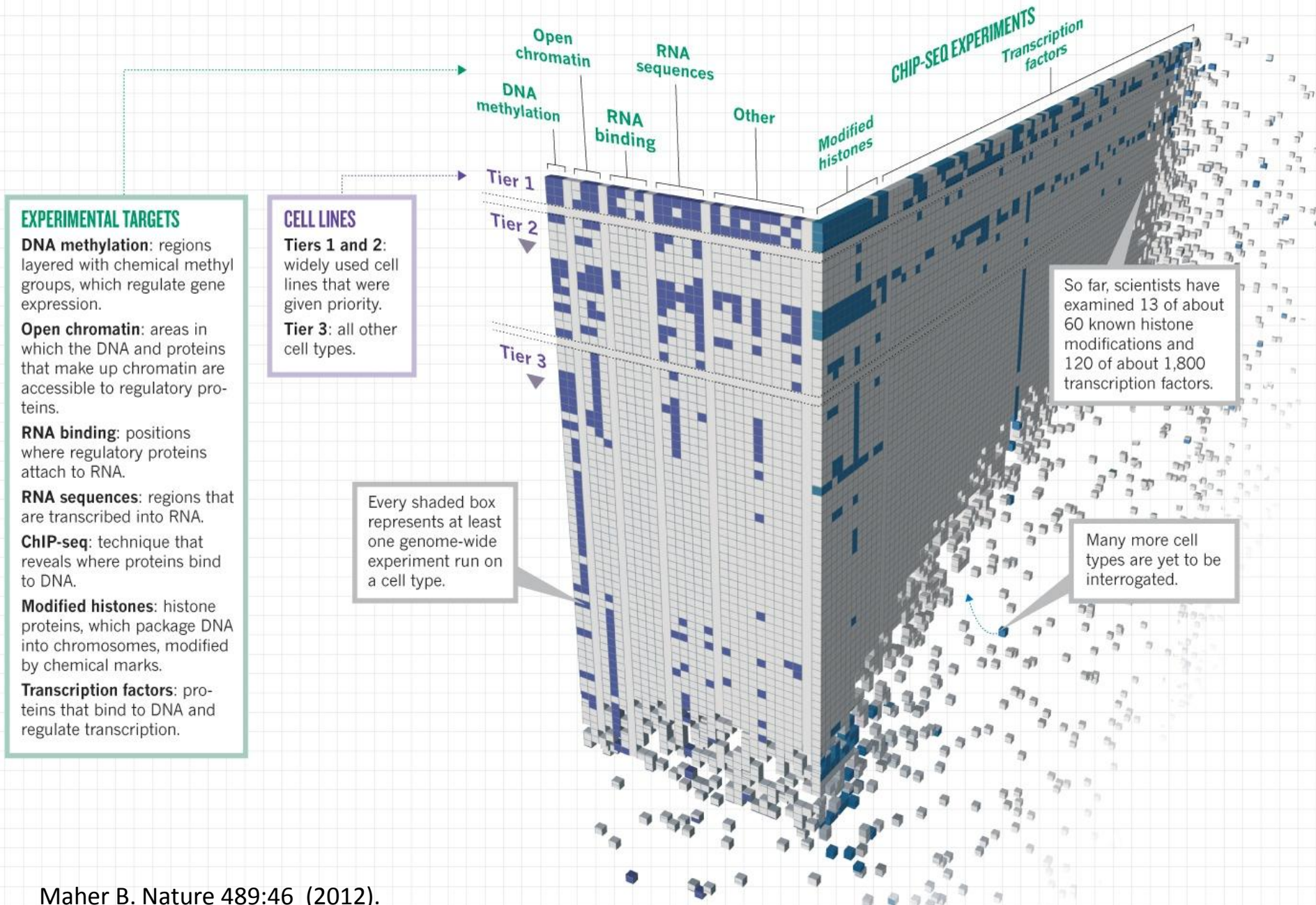
Why is the proteome so large?
Post translational modification

Beyond the Sequence: The ENCODE Project

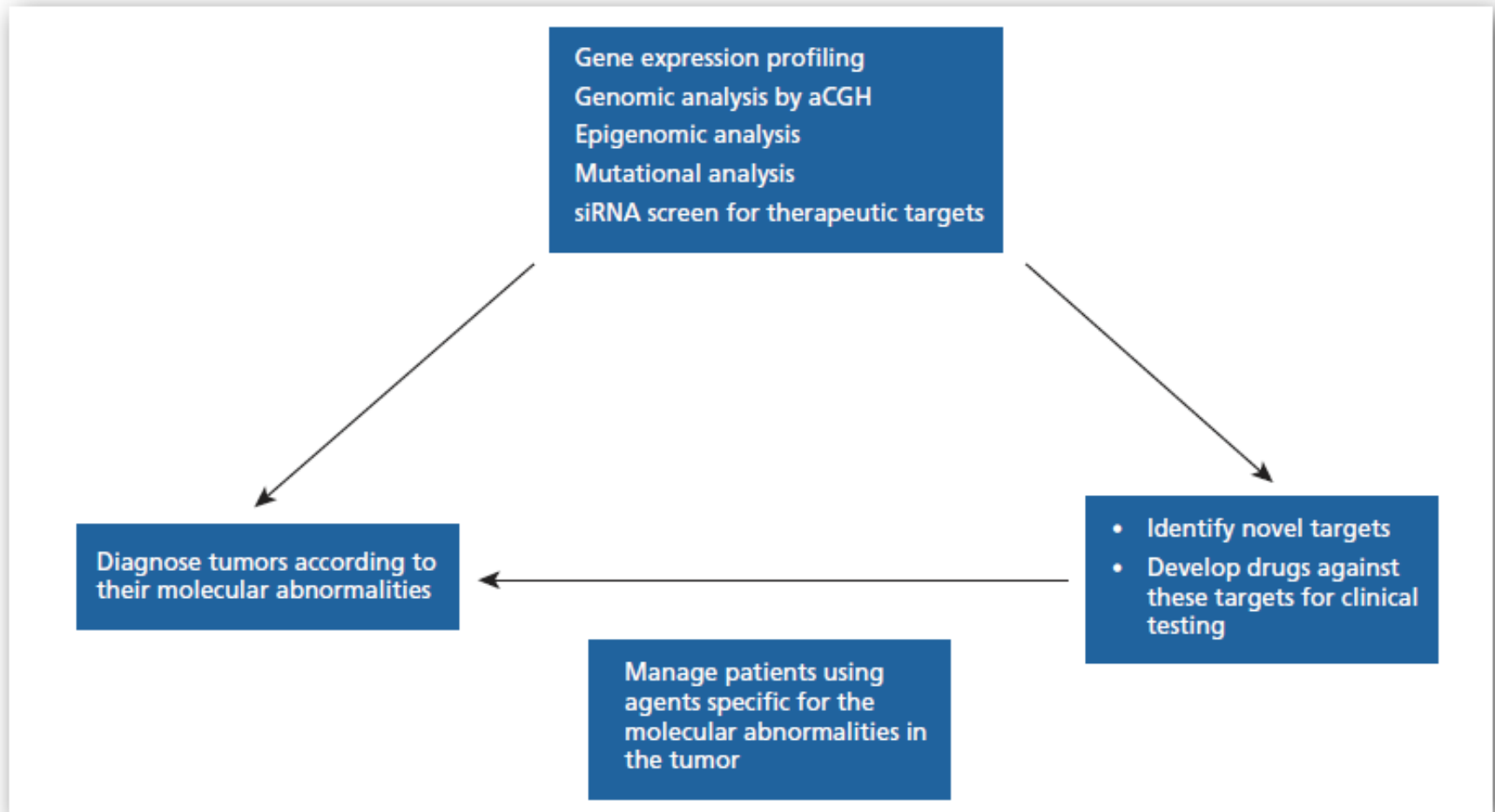


MAKING A GENOME MANUAL

Scientists in the Encyclopedia of DNA Elements Consortium have applied 24 experiment types (across) to more than 150 cell lines (down) to assign functions to as many DNA regions as possible — but the project is still far from complete.

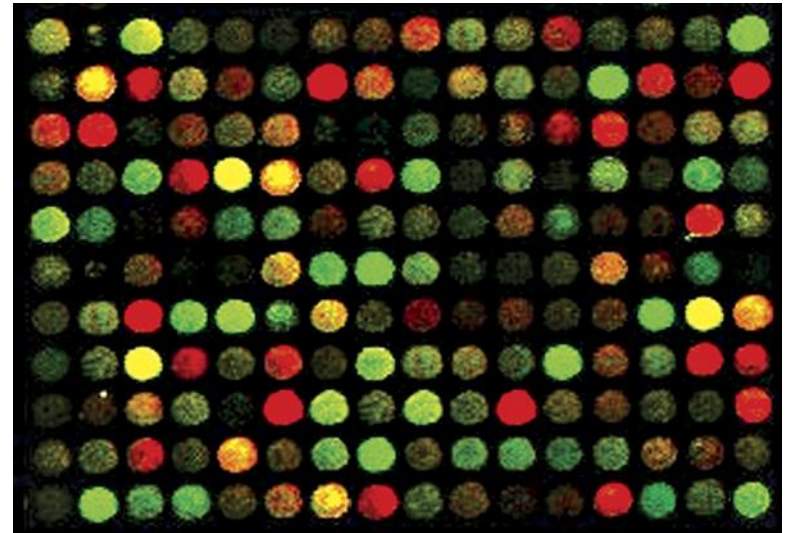


Goal of Genomic Investigations

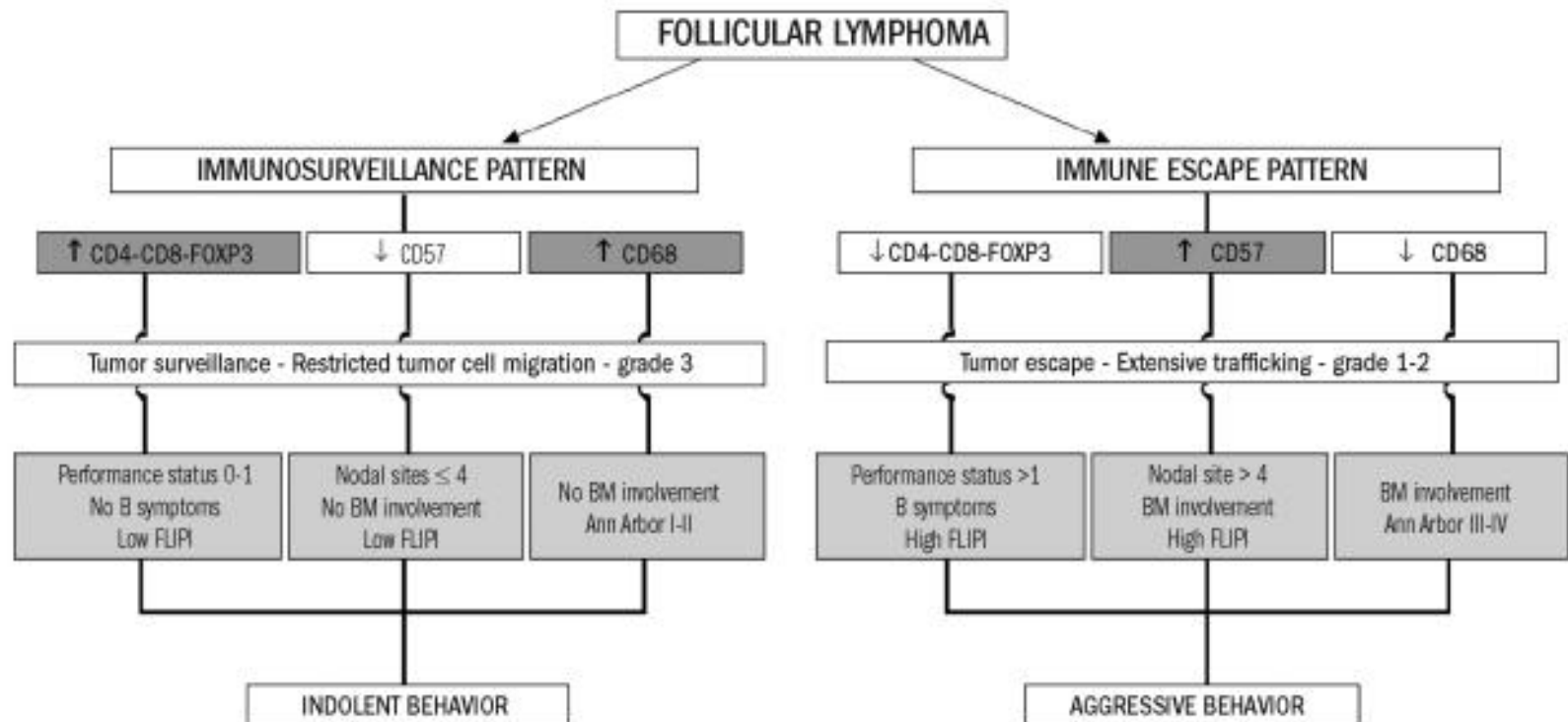


Basics of microarrays

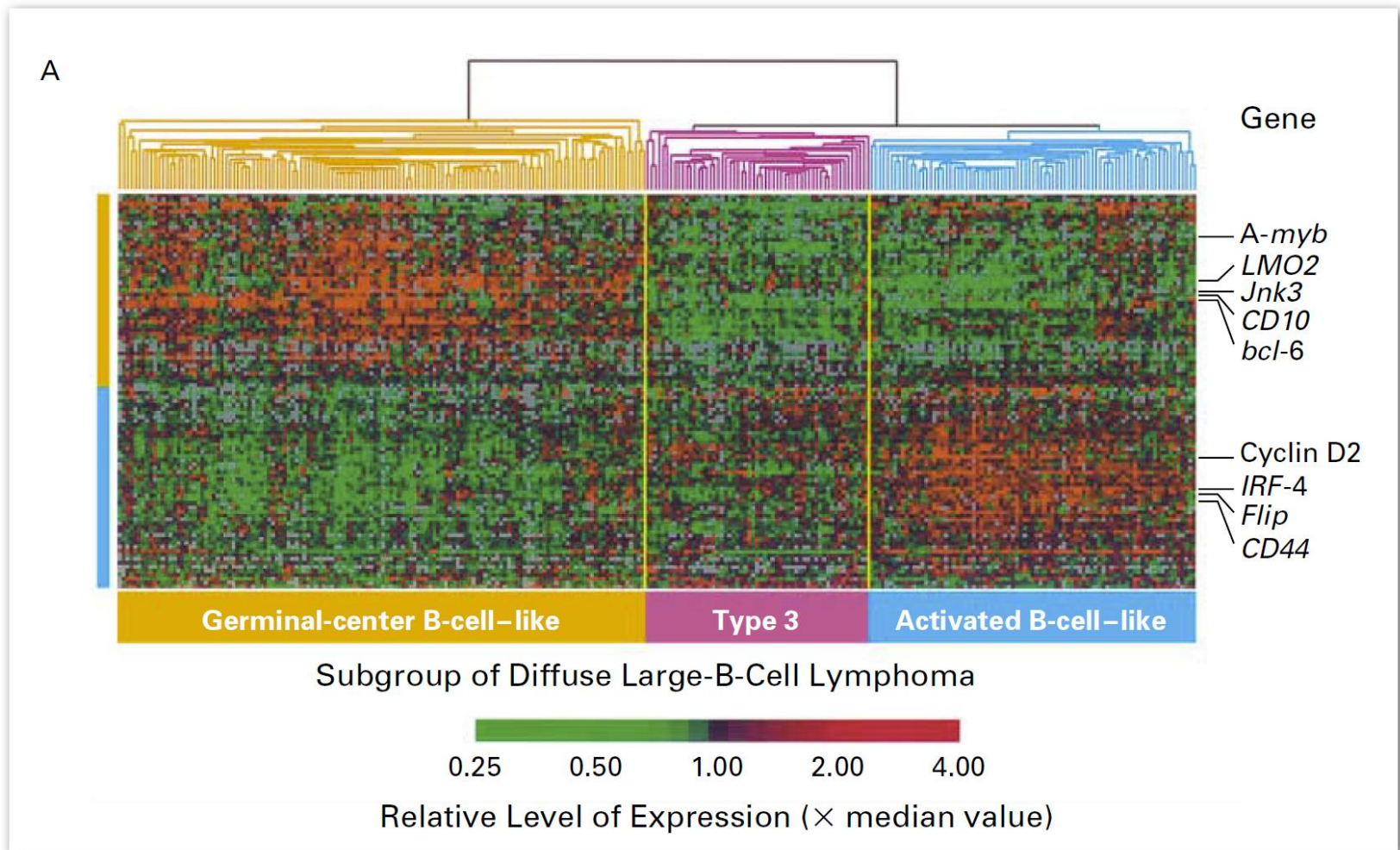
- DNA attached to solid support
 - Glass, plastic, or nylon
- RNA is labeled
 - Usually indirectly
- Bound DNA is the probe
 - Labeled RNA is the “target”



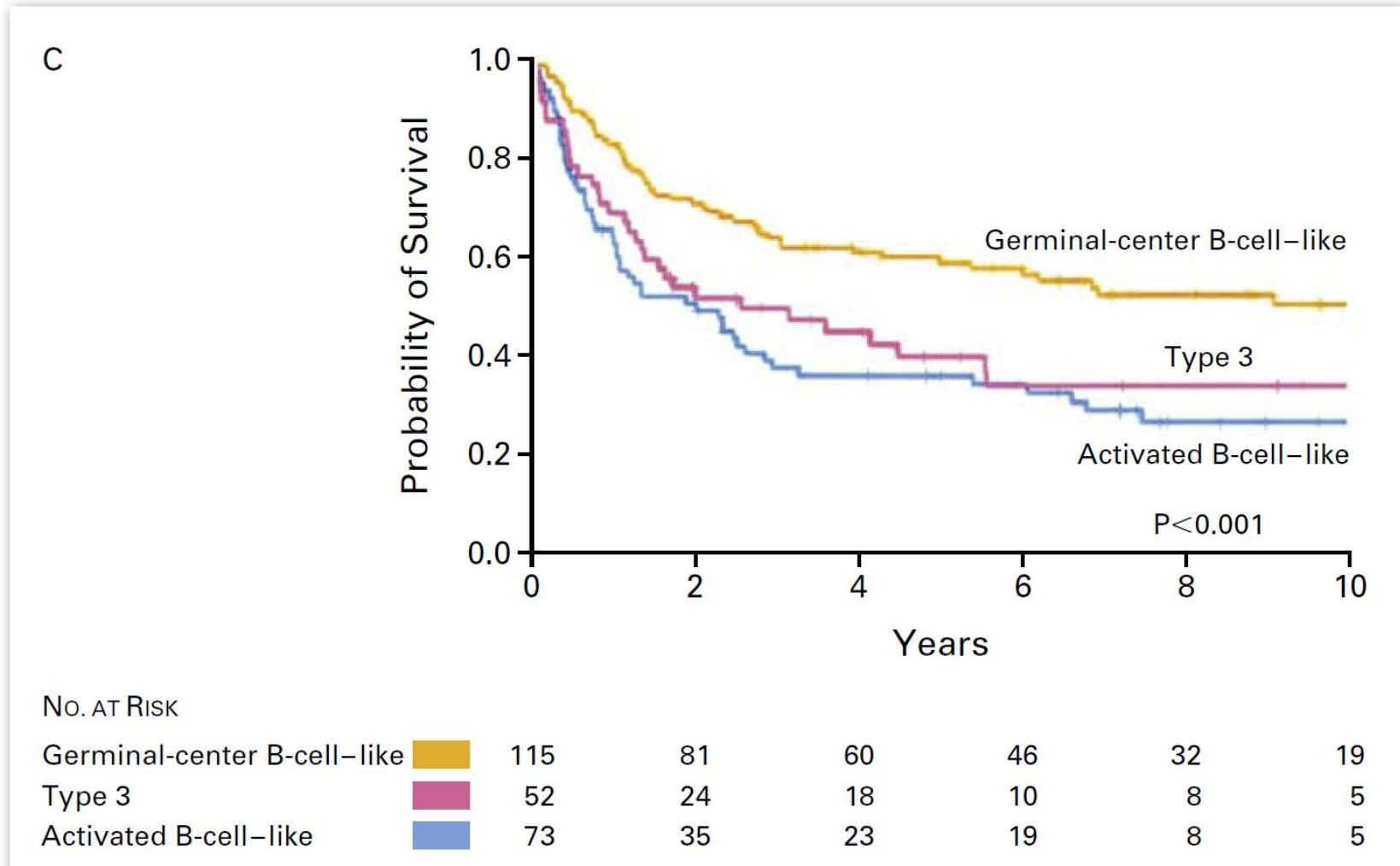
Two Immune Patterns in Follicular Lymphoma



Gene-Expression Profiles in Diffuse Large B-Cell Lymphoma



Overall Survival According to Subgroup of Diffuse Large B-Cell Lymphoma



Three Types of DLCL by Molecular Profiling

GCB	ABC	PMBL
Germinal Center B-Cell Like	Activated B-Cell Like	Primary Mediastinal B-Cell Lymphoma
t(14;18) Amp c-rel	Activation NF-kappa B bcl-2 +ve	PDL2 Overlap HL
5 yr OS 59%	5 yr OS 30%	5 yr OS 64%

A Randomised Evaluation of Molecular Guided Therapy for Diffuse Large B-cell Lymphoma With Bortezomib (REMoDL-B)

This study is currently recruiting participants.

Verified July 2011 by University Hospital Southampton NHS Foundation Trust.

Sponsor:

University Hospital Southampton NHS Foundation Trust.

Collaborator:

Janssen-Cilag Ltd.

Information provided by (Responsible Party):

University Hospital Southampton NHS Foundation Trust.

ClinicalTrials.gov Identifier:

NCT01324596

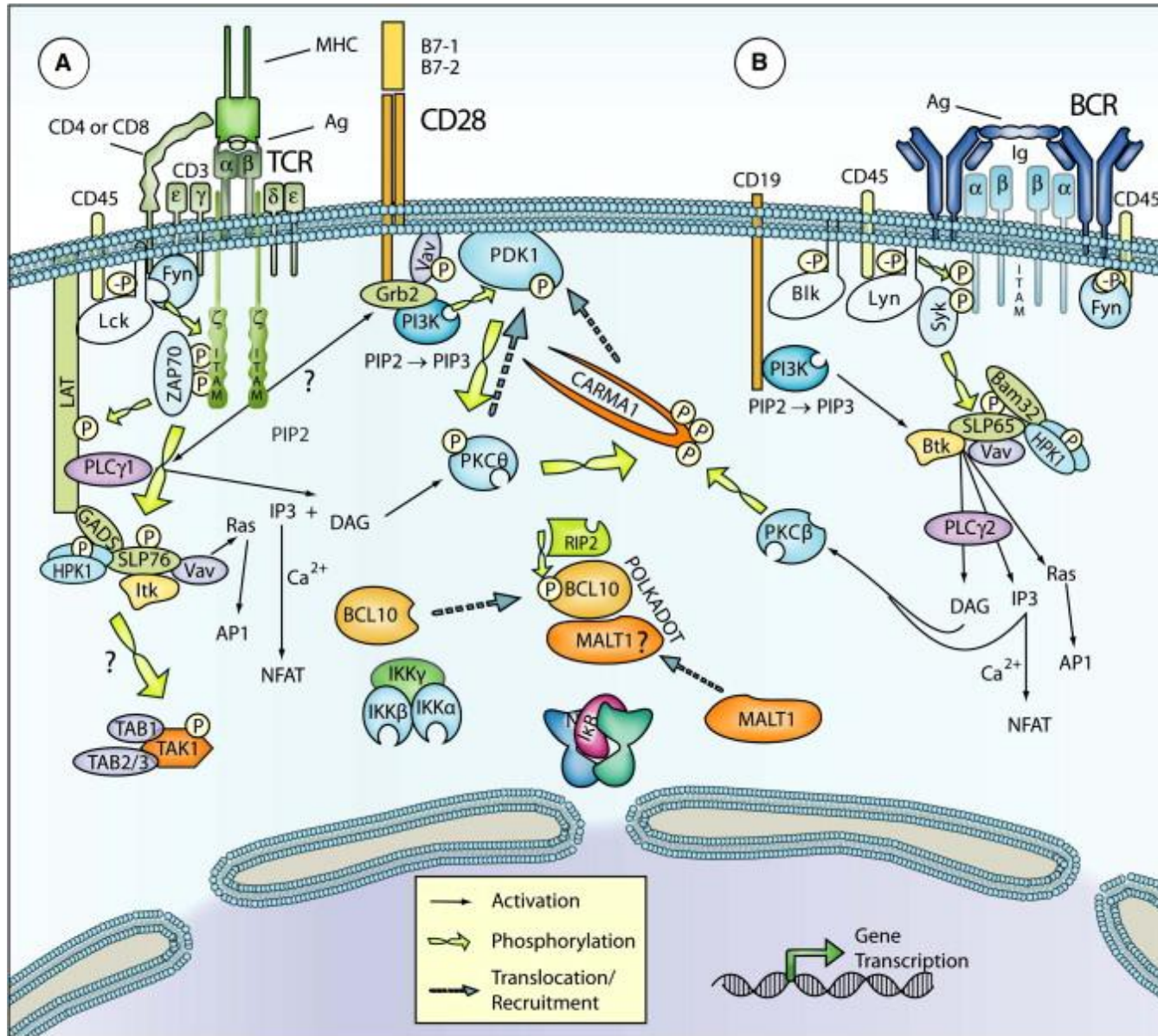
First received: March 25, 2011

Last updated: September 27, 2011

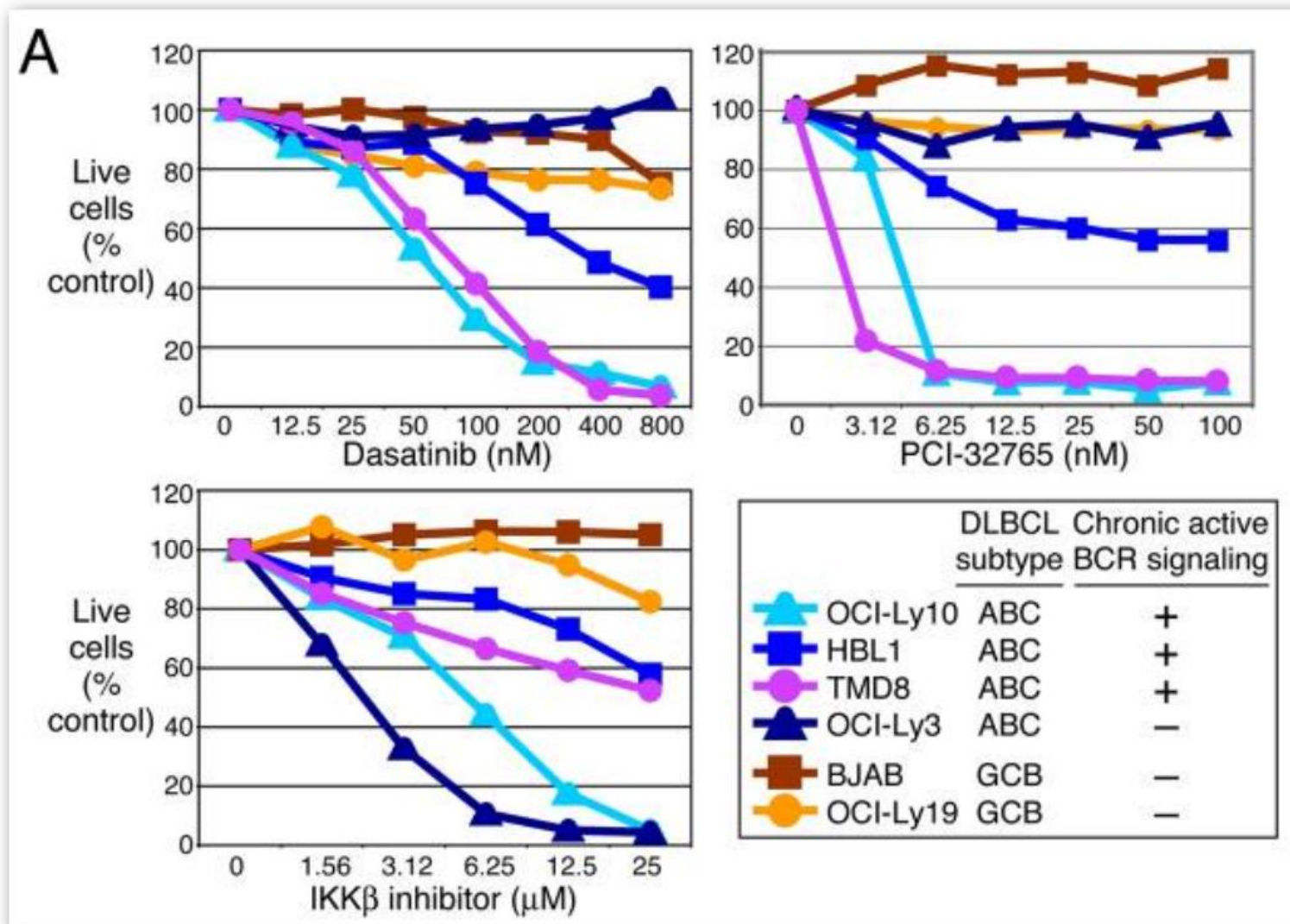
Last verified: July 2011

[History of Changes](#)

B Cell Receptor Signalling



Preclinical Testing of Inhibitors of B Cell Receptor Signalling Diffuse Large Cell Lymphoma



A Study to Evaluate the Safety and Efficacy of Dasatinib (Sprycel) in Subjects With Relapsed or Refractory Diffuse Large B-Cell Lymphoma (DLBCL)

This study is currently recruiting participants.

Verified January 2011 by Weill Medical College of Cornell University

Sponsor:

Weill Medical College of Cornell University

Collaborator:

Bristol-Myers Squibb

Information provided by:

Weill Medical College of Cornell University

ClinicalTrials.gov Identifier:

NCT00918463

First received: March 10, 2009

Last updated: January 3, 2011

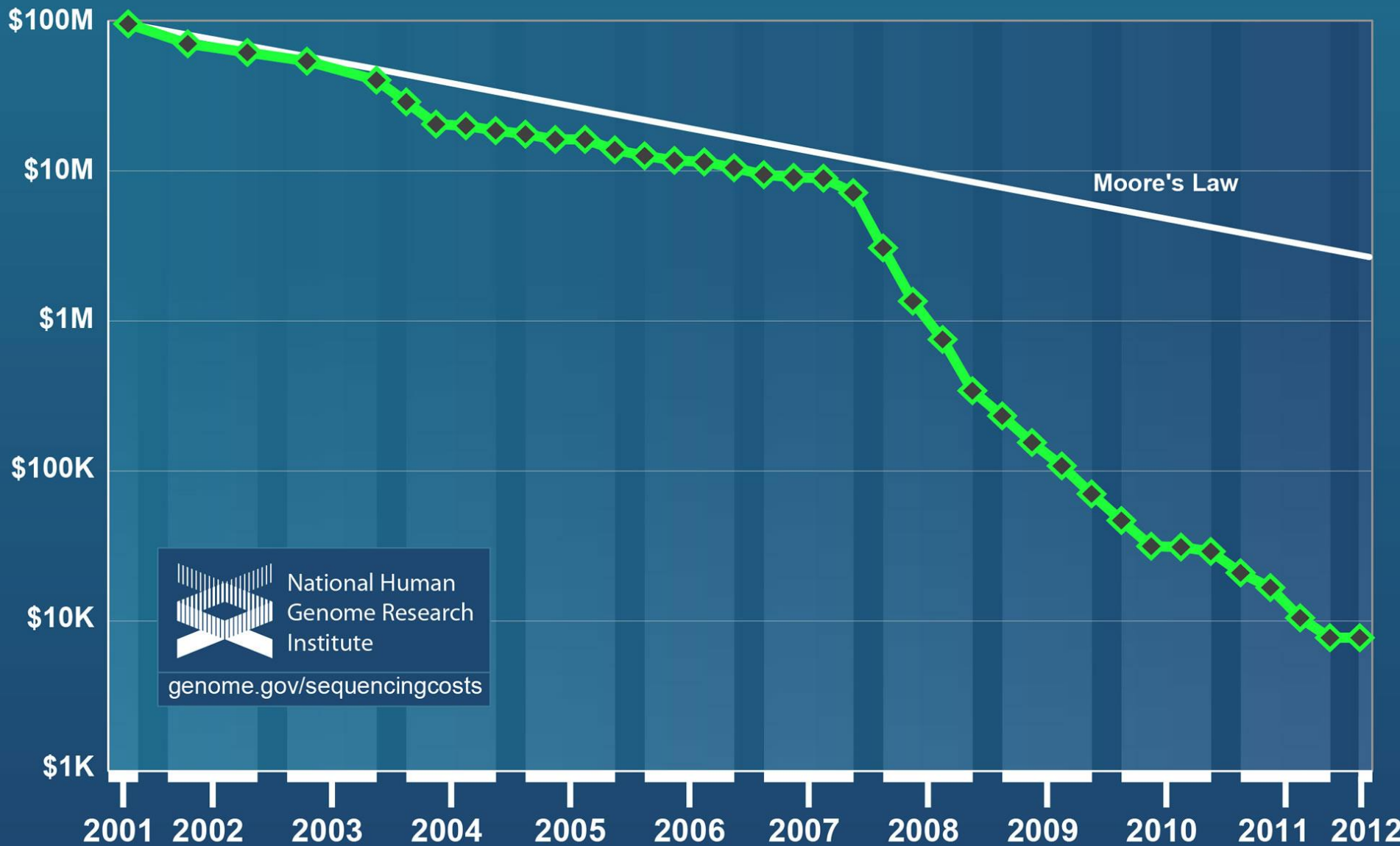
Last verified: January 2011

[History of Changes](#)

Table 1 Examples of Clinically Relevant Observations From Gene Expression Profiling Studies

Disease	Insights
Diffuse large B-cell lymphoma	<ul style="list-style-type: none">• Recognition of germinal center B, activated B, and mediastinal B subtypes^{1,2,67}• Importance of host-tumor interaction in predicting treatment outcome²⁰• Recognition of the importance of the nuclear factor-κB pathway in activated B-cell and mediastinal large B-cell subtypes, and performance or design of early pathway-directed clinical trials^{23,25}• Finding that children usually have the germinal center B subtype^{13,14}• Demonstration of a biologic difference between diffuse large B-cell lymphoma leg type and other cutaneous large B-cell lymphomas¹⁵
Mantle cell lymphoma	<ul style="list-style-type: none">• Finding that cyclin D1-negative and -positive cases express the same genomic signature²⁶
Follicular lymphoma	<ul style="list-style-type: none">• Finding that the type of tumor stromal response has a major impact on treatment outcome³¹• Identification of patients with grade 3b follicular lymphoma whose gene expression profile is different from that of patients with grades 1, 2, and 3a follicular lymphoma and whose clinical course is similar to that of patients with diffuse large B-cell lymphoma³⁰
Burkitt lymphoma	<ul style="list-style-type: none">• Demonstration that molecularly defined Burkitt lymphoma requires very intensive regimens for optimal treatment outcome³⁵
Peripheral T-cell lymphoma	<ul style="list-style-type: none">• Support for ALK-positive and -negative anaplastic large cell lymphomas being 2 different biologic entities^{38,39}• Finding that angioimmunoblastic T-cell lymphoma seems to arise in a follicular helper T cell^{39,40}• Recognition that some peripheral T-cell lymphoma not otherwise specified can be reclassified into angioimmunoblastic T-cell lymphoma and a spectrum of cytotoxic T-cell lymphomas³⁹
Waldenstrom's macroglobulinemia	<ul style="list-style-type: none">• Finding that gene expression more closely resembles chronic lymphoma leukemia than multiple myeloma⁶⁸

Cost per Genome



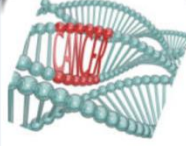
Personal Genomics

otogenetics homepage

Exome NGS Services RNA-Seq Services Other Services/Products Contact Us About Otagenetics Corporation


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Predefined Disease or pathway Genes




Cancer, Deafness, Heart Diseases, ADME genes,..... NGS of selected targets allows high coverage

Human & Mouse Exome NGS



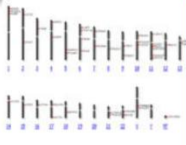
Lowest Price on the market for human exome sequencing. Guaranteed in writing. From \$698/sample.

Epigenetic Profiling Services




Genome-wide profiling of epigenetically modified DNA for cancer and stem cell biology, and more.

Custom Targeted NGS sequencing



You provide gene target lists, we will capture & sequence up to 20M bps. Many species are included.

RNA-Seq

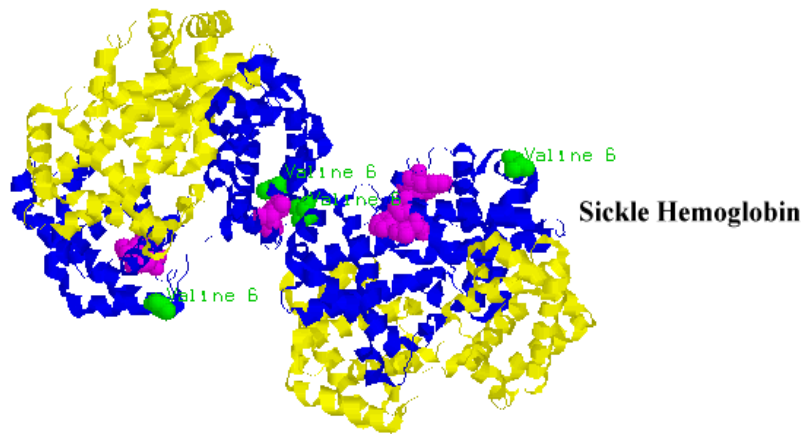
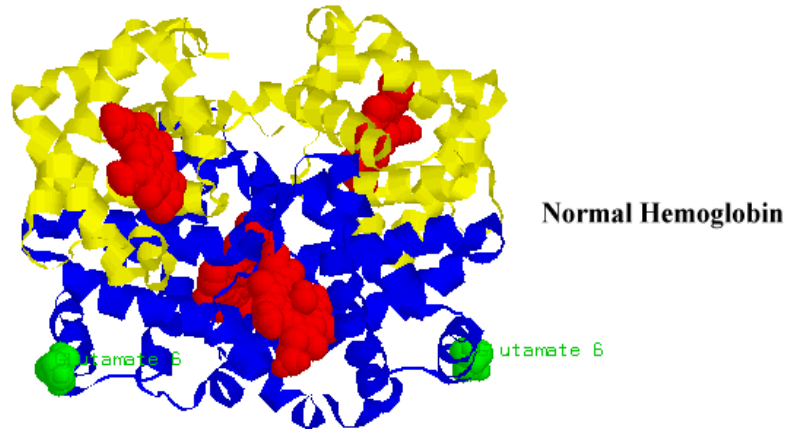


High-quality RNA-Seq from \$698/sample. At a cost less than the microarrays, you can do much more with the RNA-seq data

400 Pinnacle Way, Ste 435, Norcross, GA30071, USA. sales@otogenetics.com Tel (toll free): 855-otogene (686-4363); Fax: 206-339-8150

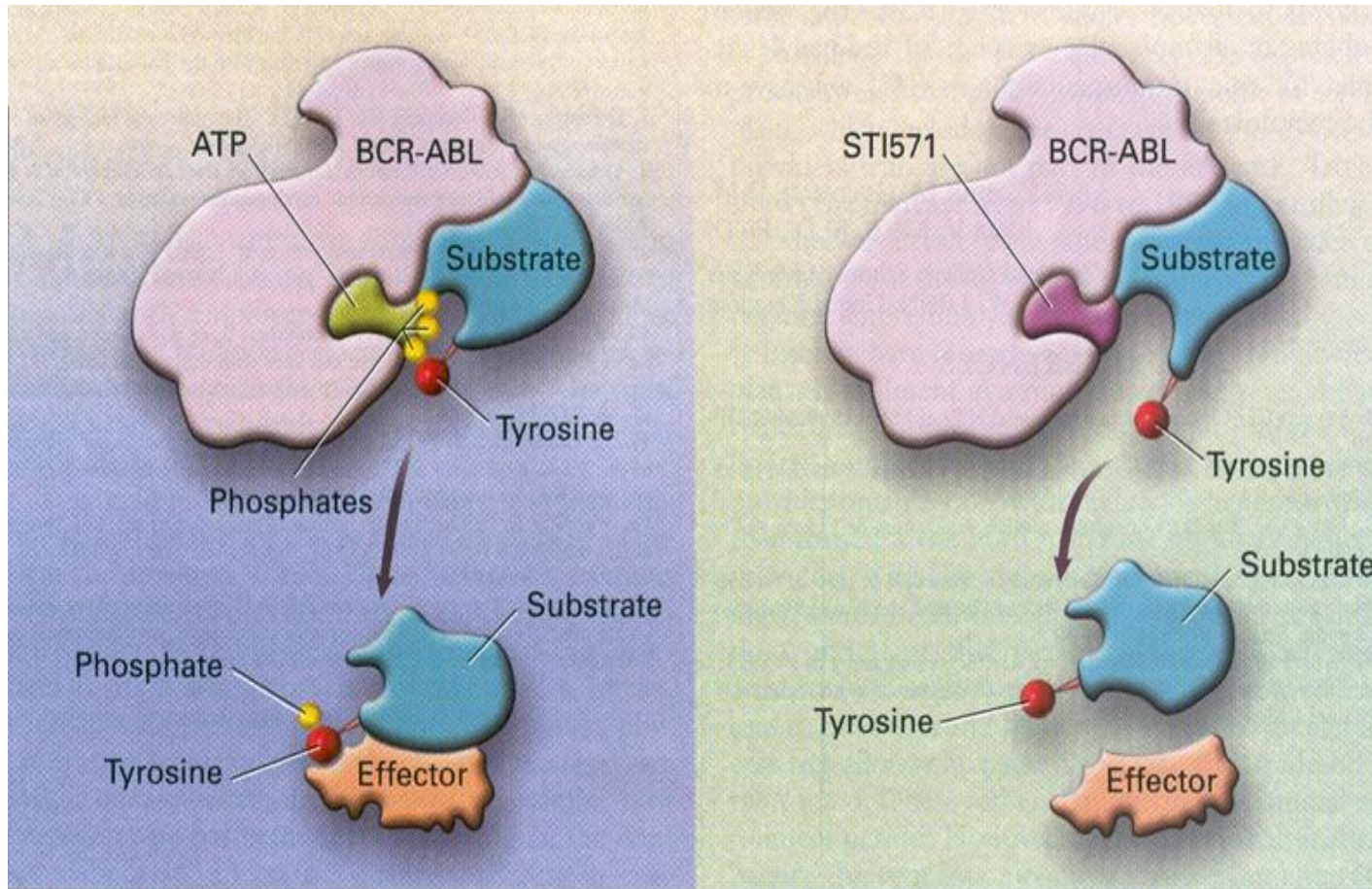
4:22 AM 11/12/2012

Sickle Cell Anemia



Note: The Sickle hemoglobin image is drawn at 50% of the size of the Normal hemoglobin

Mechanism of Action of Imatinib Mesylate



Summary

- Advances
 - Recognition of new clinically relevant subtypes
 - Recognition of new “drugable” targets
- Disappointments
 - Genome more complicated than imagined
 - Less therapeutic insights than hoped for
- Personal Genomics
 - Not ready for prime time...but likely in the future