

Molecular Diagnostics for T-cell Lymphomas

David Weinstock, MD



DISCLOSURES

Research Support;

Daiichi Sankyo
Verastem
Abcuro

Consulting;

Bantam
ASELL
Secura
Biopharma
AstraZeneca

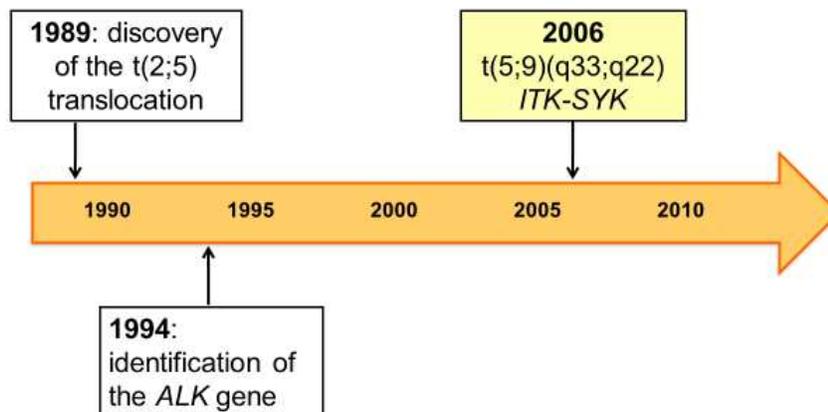
Founder;

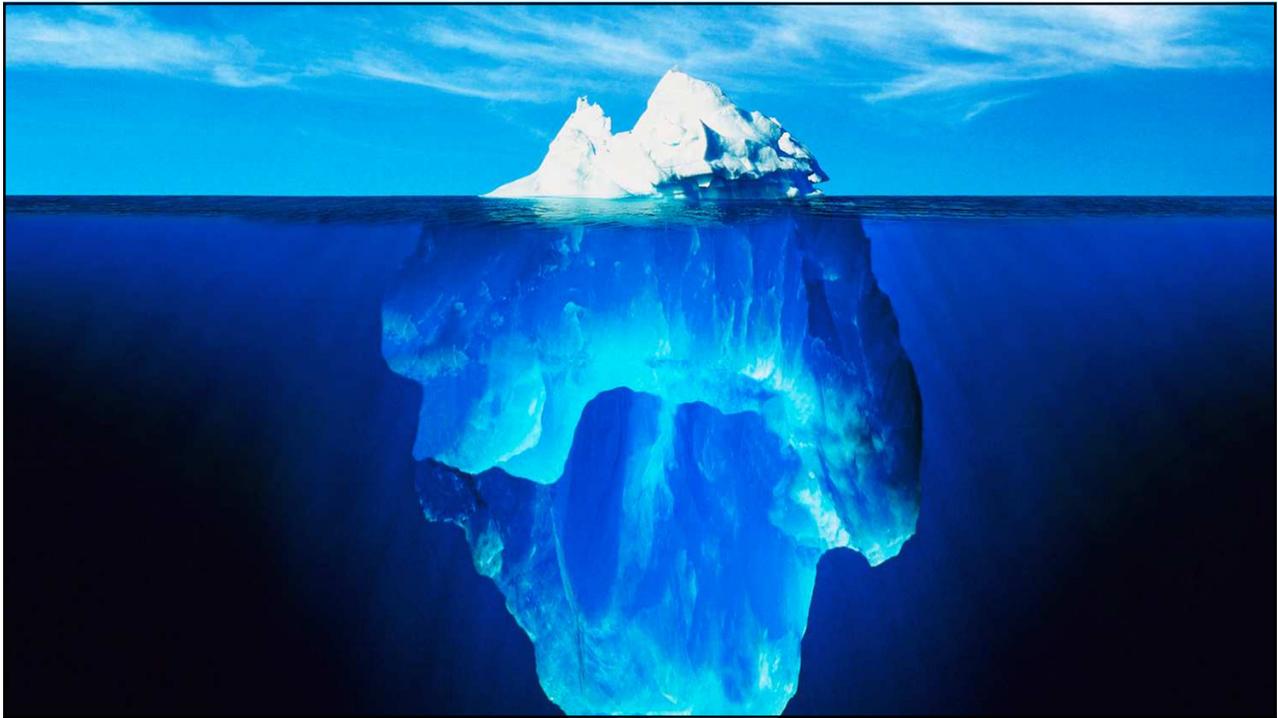
Travera
Ajax
Root



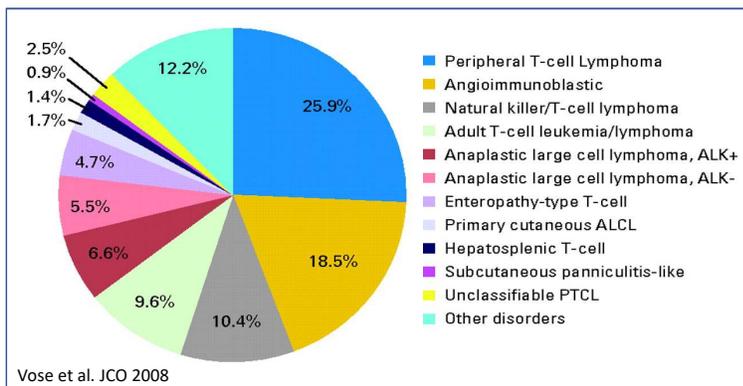
**Tricky and Terrible T-cell Tumors:
These Are Thrilling Times for Testing
Molecular Pathology of Peripheral T-Cell Lymphomas**

Novel chromosomal translocations in PTCLs

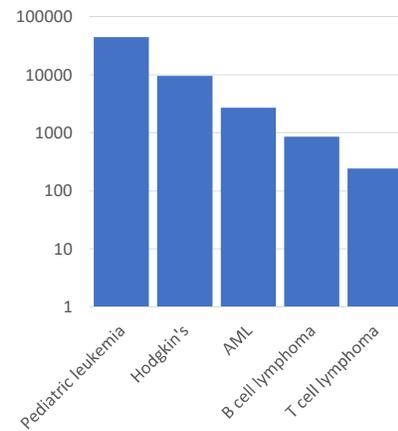




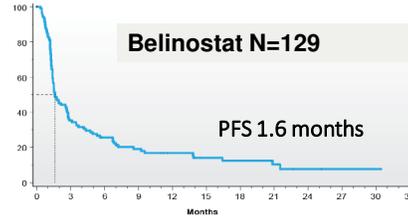
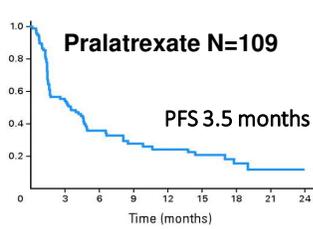
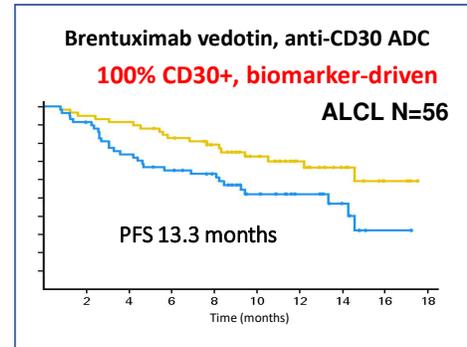
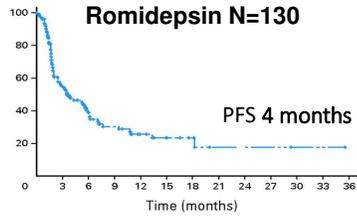
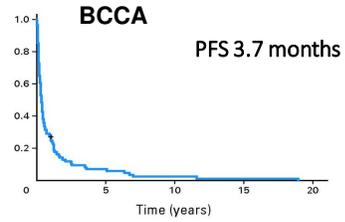
Challenges to progress in T-cell lymphomas



Google hits/death in US annually



Therapeutic crawl



Mak V et al. JCO 2013;31:1970-1976, O'Connor OA, et al. J Clin Oncol. 2011;29:1182-1189, Coiffier B, et al. J Clin Oncol. 2012;30 :631-636, O'Connor OA et al ASCO 2013, Pro B, et al. J Clin Oncol. 2012;30:2190-2196, Horwitz SM et al. Blood 2014;123:3095-3100

Hypotheses

1. Better understanding of TCL genomics can guide the development of therapies for populations
2. Sequencing a TCL can guide therapeutic selection for an individual patient



Case

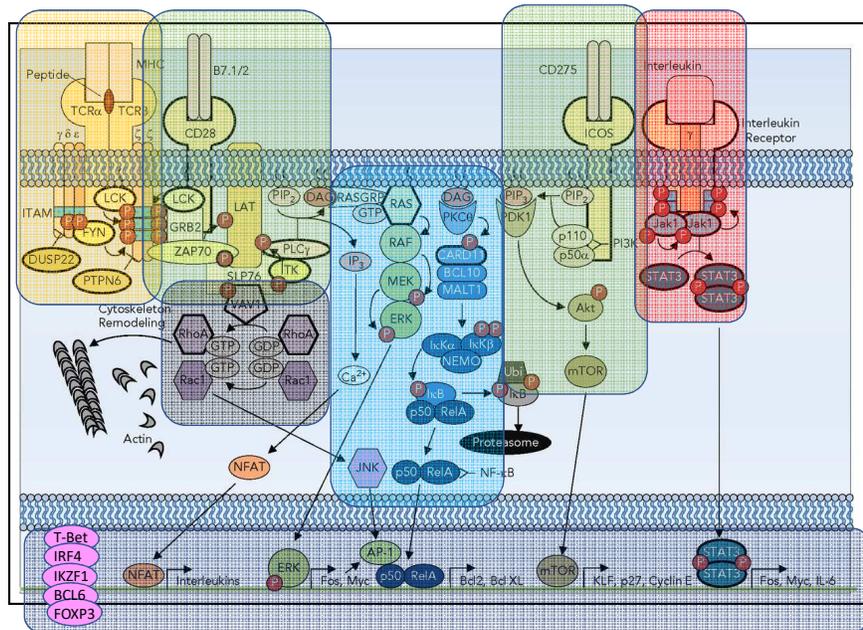
58 year old woman with no other medical problems:

- Stage IV PTCL-NOS
- Treated with CHOEP chemotherapy and then an autologous stem cell transplant
- Relapsed after 12 months with bone marrow and nodal involvement

How likely are you to order next-generation sequencing analysis?

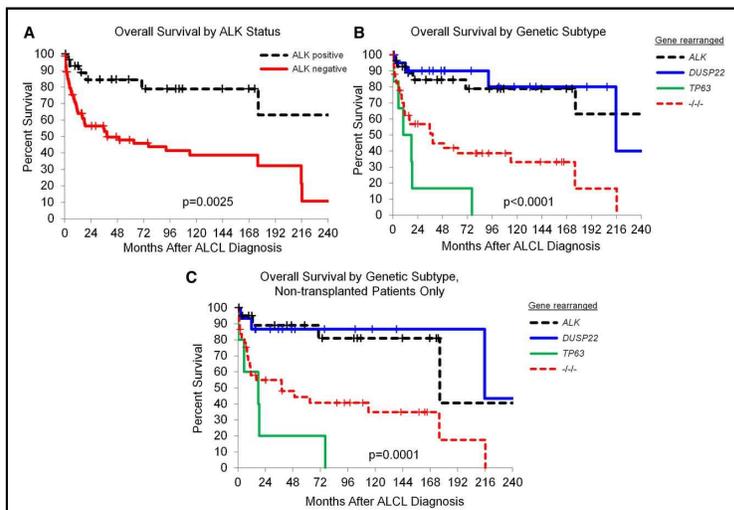
- A** Never
- B** Rarely (<25% of the time)
- C** Sometimes (26-75%)
- D** Usually (>75%)
- E** Always

...but there are some commonalities

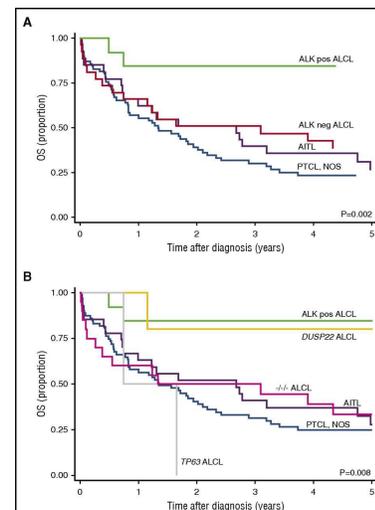


Van Arnam JS, Lim MS, Elenitoba-Johnson KS. *Blood*. 2018;131(21):2320-2330.

ALCL genomics were prognostic

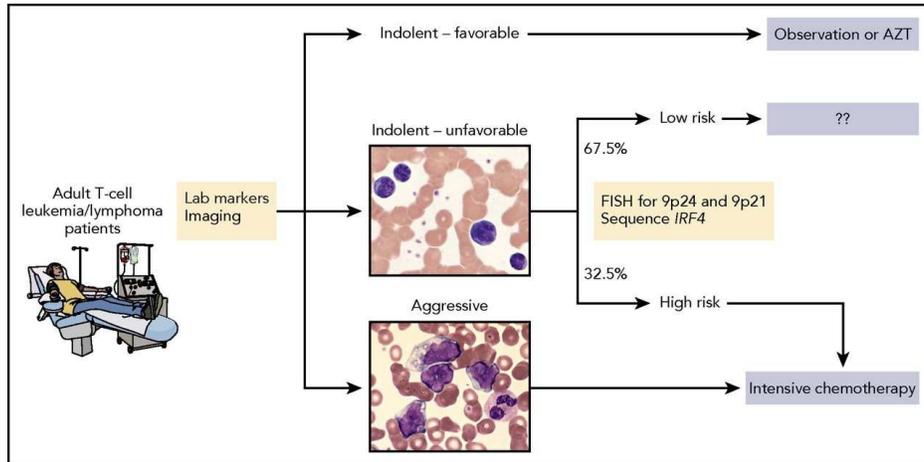


Castellar et al. *Blood* 2014;124:1473-1480



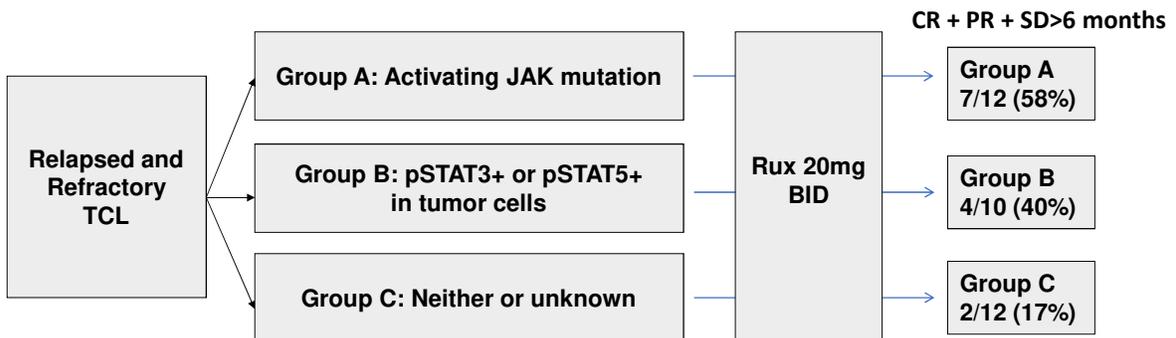
Pedersen et al. *Blood* 2017;130:554-557

ATLL genomics identified a low-risk group

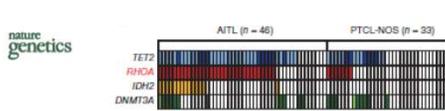


Kataoka et al. Blood 2018;131:215-225; Yoshida and Weinstock Blood 2018;131:159-160

Ruxolitinib for T-cell lymphomas with JAK/STAT alterations: maybe?

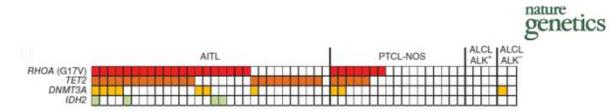


Targeting lymphomas with mutated epigenetic modulators: perhaps?



Somatic *RHOA* mutation in angioimmunoblastic T cell lymphoma

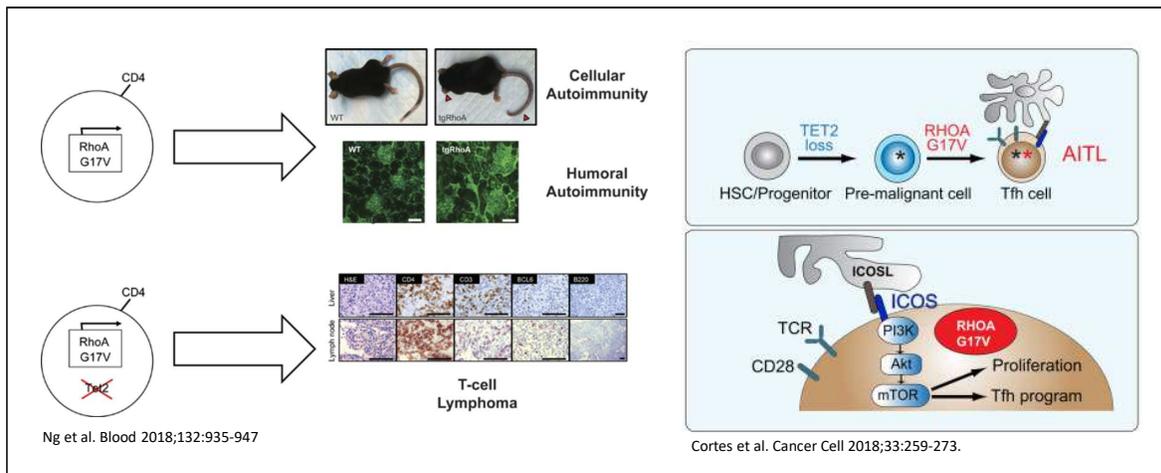
Mamiko Sakata-Yanagimoto^{1,2,3}, Terukazu Enami^{1,2,3}, Kenichi Yoshida^{3,4,5,6,7}, Yuichi Shiraiishi⁸, Ryohel Ishii⁹, Yasuyuki Miyake¹, Hideharu Muto¹, Naoko Tsuyama⁸, Aiko Sato-Otsubo^{3,5}, Yusuke Okuno⁸, Seiji Sakata¹, Yuki Kanada¹, Rie Nakamoto-Matsubara¹, Ngyeny Richi Tsai¹, Koji Inoue^{9,2}, Yusuke Sato^{3,5}, Yasunori Ohta¹⁰, Junichi Furuta¹, Seichi Shimizu¹², Takuya Kemeno¹³, Yuji Sato¹⁴, Takayoshi Ito¹⁵, Masayuki Noguchi¹⁶, Emiko Noguchi¹⁷, Masashi Sanada^{3,5}, Kenichi Chiba⁴, Hiroko Tanaka¹⁸, Kazumi Suzukawa¹⁹, Toru Nannooki¹⁹, Yuichi Hasegawa¹, Osamu Nureki¹, Satoru Miyano^{4,18}, Naoya Nakamura²⁰, Kengo Takeuchi^{6,7}, Seishi Ogawa^{21,22} & Shigeru Chiba^{21,23}

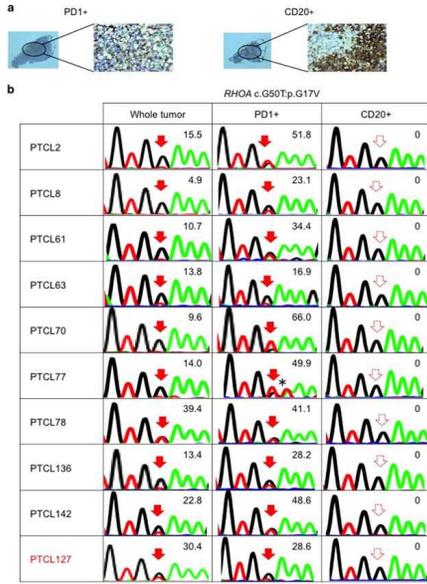


Recurrent mutations in epigenetic regulators, *RHOA* and *FYN* kinase in peripheral T cell lymphomas

Teresa Palomero^{1,2,19}, Lucile Couronne^{1,19}, Hossein Khiabanian^{3,19}, Mi-Yeon Kim¹, Alberto Ambesi-Impiombato¹, Arienne Perez-Garcia¹, Zachary Carpenter³, Francesco Abate^{3,4}, Maddalena Allegretta¹, J Erika Haydu¹, Xiaoyu Jiang⁵, Izidore S Loscos^{5,6}, Concha Nicolas⁷, Milagros Balbin⁸, Christian Bastard⁹, Govind Bhagat², Miguel A Piris^{10,11}, Elias Campo^{12,13}, Olivier A Bernard¹⁴⁻¹⁶, Raul Rabadan^{3,17} & Adolfo A Ferrando^{1,2,18}

Tet2 loss directly contributes to T_{FH}-cell transformation

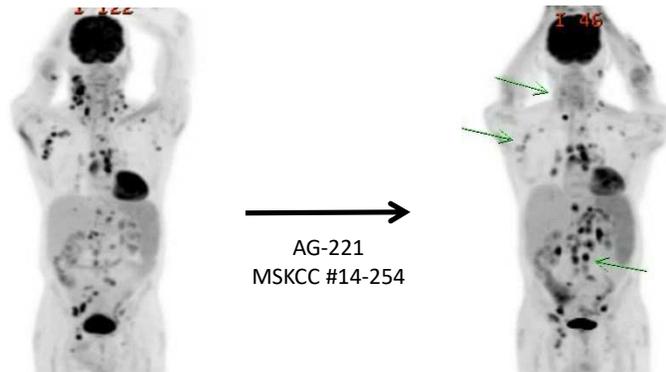




	TET2			DNMT3A			RHOA		IDH2		NOTCH1		IGH VDJ status
	whole tumor	PD1+	CD20+	whole tumor	PD1+	CD20+	whole tumor	PD1+	whole tumor	PD1+	whole tumor	PD1+	
PTCL2	1.5	86.6	4.9	30.6	22.2	41.5	15.5	51.8					
PTCL8	6.8	51.4	28.7	5.6	27.9		4.9	23.1	5.5	22.7			
PTCL60	10.0	36.4	47.5	11.5	48.6	6.2							
PTCL61	42.1	27.8	36.1				10.7	34.4	9.1	26.9			
PTCL63	17.1	29.1	11.7				13.8	16.9	12.2	15.6	17.4	100	OC
PTCL70	30.6	31.6	45.1	35.7	14.7		9.6	66.0	8.2	30.3			
PTCL74				2.4	27.9						22.4	100	MC
PTCL77	13.8	41.6	24.8				14.0	49.9					
PTCL78	64.5	79.7					39.4	41.1			23.7	40.3	OC
PTCL80	32.5	73.3	100										
PTCL136	28.0	23.9	44.9	41.3	56.9	15.7	13.4	28.2					
PTCL142	20.2	27.3	54.5				22.8	48.6					

Nguyen et al. Blood Cancer J 2017;7:e516

IDH2 inhibition for IDH2-mutated lymphoma: useful?



Targeting epigenetic regulators in AITL



TO THE EDITOR:

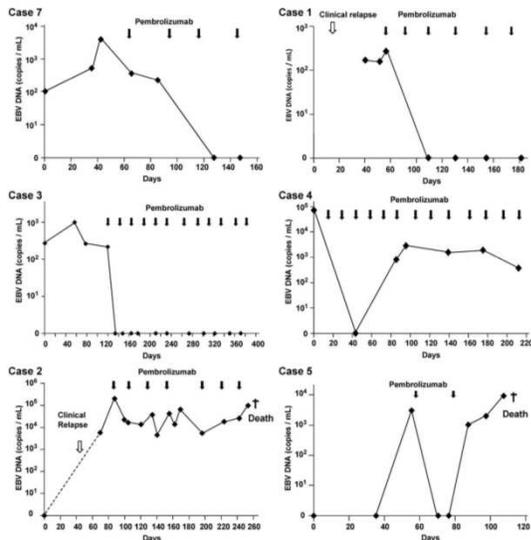
Treatment with 5-azacytidine induces a sustained response in patients with angioimmunoblastic T-cell lymphoma

François Lemonnier,¹⁻³ Jehan Dupuis,¹ Pierre Sujobert,^{4,5} Olivier Tournilhac,⁶ Morgane Cheminant,^{7,9} Clémentine Sarkozy,^{5,10} Laura Pelletier,⁷ Ambroise Marçais,^{7,9} Cyrielle Robe,³ Virginie Fataccioli,^{3,11} Corinne Haicou,¹⁻³ Olivier Hermine,^{7,9} Philippe Gaulard,^{2,3,11,*} and Richard Delarue^{2,9,*}

¹Unité Hémopathies Lymphoïdes, Hôpitaux Universitaires Henri Mondor, Assistance Publique des Hôpitaux de Paris, Créteil, France; ²Université Paris-Est Créteil, Créteil, France; ³Institut Mondor de Recherche Biomédicale, INSERM U955, Créteil, France; ⁴Hospices Civils de Lyon, Service d'Hématologie Biologique, Pierre Bénite, France; ⁵INSERM 1052, CNRS 5286, Université Claude Bernard, Faculté de Médecine Lyon-Sud Charles Mérieux, Université de Lyon, Pierre Bénite, France; ⁶Service d'Hématologie Clinique Adulte et de Thérapie Cellulaire, CHU Clermont-Ferrand, Clermont-Ferrand, France; ⁷Service d'Hématologie Adultes, Hôpital Necker, Assistance Publique des Hôpitaux de Paris, Paris, France; ⁸Université Paris Descartes, Paris, France; ⁹INSERM UMR 1163, CNRS ERL 8254, Laboratory of Cellular and Molecular Mechanisms of Hematological Disorders and Therapeutic Implications, Imagine Institute, Paris, France; ¹⁰Service d'Hématologie Clinique, Hospices Civils de Lyon, Hôpital Lyon Sud, Pierre Bénite, France; and ¹¹Département de Pathologie, Hôpitaux Universitaires Henri Mondor, Assistance Publique des Hôpitaux de Paris, Créteil, France

No association between response and TET2 mutation status

Genomics may predict response to PD-1/PD-L1 blockade



Kwong et al. Blood 2017;129:2437-2442

LETTER

doi:10.1038/nature18294

Aberrant *PD-L1* expression through 3'-UTR disruption in multiple cancers

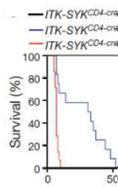
Keisuke Kataoka^{1*}, Yuichi Shiraiishi^{2*}, Yohei Takeda^{3*}, Seiji Sakata⁴, Misako Matsumoto⁵, Seiji Nagano⁶, Takuya Maeda⁴, Yasunobu Nagata¹, Akira Kitanaka⁶, Seiya Mizuno⁷, Hiroko Tanaka², Kenichi Chiba², Satoshi Ito², Yosaku Watatani⁸, Nobuyuki Kakiuchi⁹, Hiromichi Suzuki¹⁰, Tetsuichi Yoshizato¹, Kenichi Yoshida¹, Masashi Sanada⁸, Hidehiro Itonaga⁹, Yoshitaka Imaizumi¹⁰, Yasushi Totoki¹¹, Wataru Munakata¹², Hiromi Nakamura¹³, Natsuko Hama¹³, Kotaro Shide⁶, Yoko Kubuki⁶, Tomonori Hidaka⁶, Takuro Kameda⁶, Kyoko Masuda⁶, Nagahiro Minato¹³, Koichi Kashiwase¹⁴, Koji Izutsu¹⁵, Akifumi Takaori-Kondo¹⁶, Yasushi Miyazaki¹⁰, Satoru Takahashi⁷, Tatsuhiko Shibata^{17,18}, Hiroshi Kawamoto¹, Yoshiki Akatsuka^{18,19}, Kazuya Shimoda², Kengo Takeuchi¹, Tsukasa Seya², Satoru Miyano² & Seishi Ogawa¹

Uninformed use of PD-1/PD-L1 blockade could hurt patients

LETTER

PD-1 is a hapl lymphomage

Tim Wartewig^{1,2}, Zsuzsanna Kung Roman Maresch^{2,4}, Thorsten Büch



Germline *HAVCR2* mutations altering TIM-3 characterize subcutaneous panniculitis-like T cell lymphomas with hemophagocytic lymphohistiocytic syndrome

Tenzin Gayden^{1,3,2}, Fernando E. Sepulveda^{2,3,2}, Dong-Anh Khuong-Quang^{3,4,3,2}, Jonathan Pratt^{1,3,2}, Elvis T. Valera^{1,5}, Alexandrine Garrigue², Susan Kelso^{6,7}, Frank Sicheri^{6,7}, Leonie G. Mikael¹, Nancy Hamel⁸, Andrea Bajic¹, Rola Dali⁹, Shriya Deshmukh¹⁰, Dzana Dervovic⁶, Daniel Schramek^{6,7}, Frédéric Guerin², Mikko Taipale⁷, Hamid Nikbakht^{1,9}, Jacek Majewski^{1,11}, Despina Moshous¹², Janie Charlebois¹³, Sharon Abish¹³, Christine Bole-Feysot¹⁴, Patrick Nitschke¹⁵, Brigitte Bader-Meunier¹², David Mitchell¹³, Catherine Thieblemont^{16,17}, Maxime Battistella^{17,18}, Simon Gravel¹¹, Van-Hung Nguyen¹⁹, Rachel Conyers^{3,4}, Jean-Sebastien Diana¹², Chris McCormack^{20,21}, H. Miles Prince^{22,23}, Marianne Besnard²⁴, Stephane Blanche¹², Paul G. Ekert^{3,4}, Sylvie Fraïtag²⁵, William D. Foulkes^{1,8}, Alain Fischer^{12,26,27}, Bénédicte Neven^{12,27,33}, David Michonneau^{17,28,33}, Geneviève de Saint Basile^{2,29,33*} and Nada Jabado^{1,30,31,33*}

emia-Lymphoma apy

d negative findings on positron-
graphy, and the second had nega-
n computed tomography, except

ent, the first patient reported
elling of skin lesions within the
kocytosis, hypercalcemia, renal
nd increased lactate dehydroge-
oped in all three patients. In two
and 30% atypical lymphocytes
; in the blood and hyperbilirubin-
ssive splenomegaly were present;
ient, marked worsening of nodal
ase was noted. The HTLV-1 provi-
ed in two patients, increased by a
nd 2.4. Patients 2 and 3 received
therapy, and Patient 1 received
skin lesions and spleen.

d colleagues recently found that
ll death 1 (PD-1) was a tumor
-cell lymphoma in a mouse mod-
nt and rapid amplification of can-
ents after a single dose of nivolu-
provides support for the probable

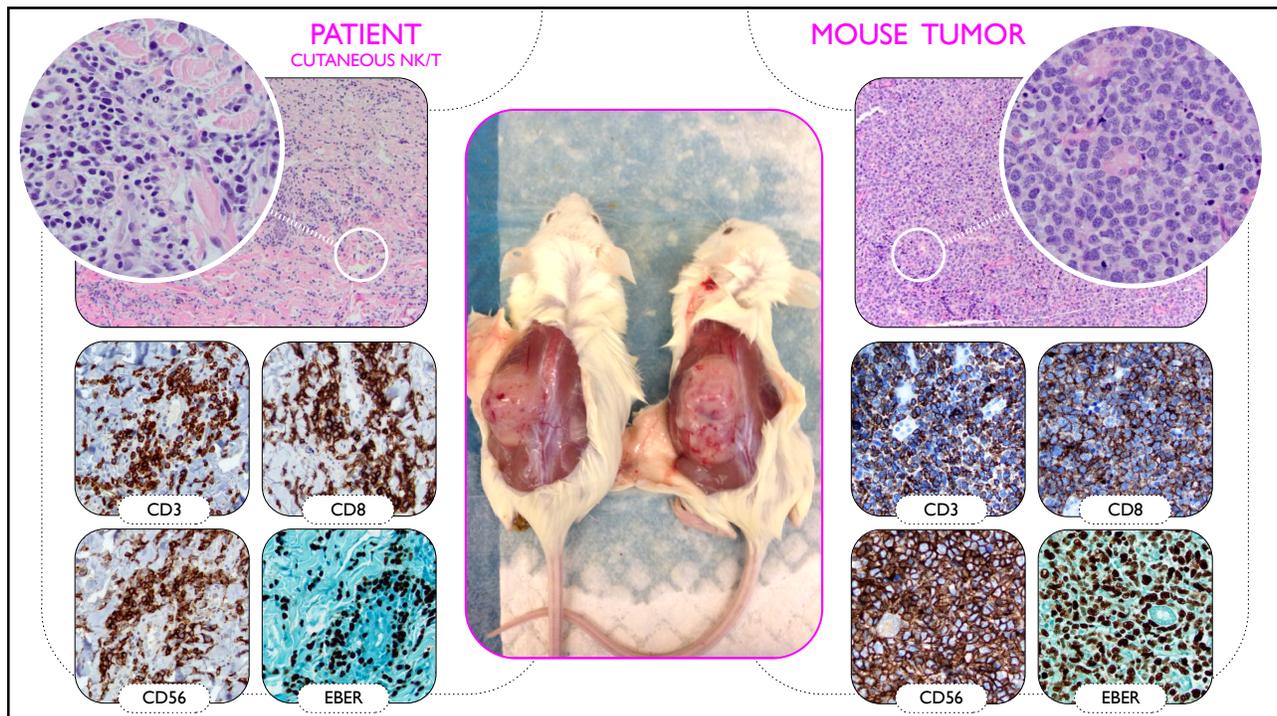
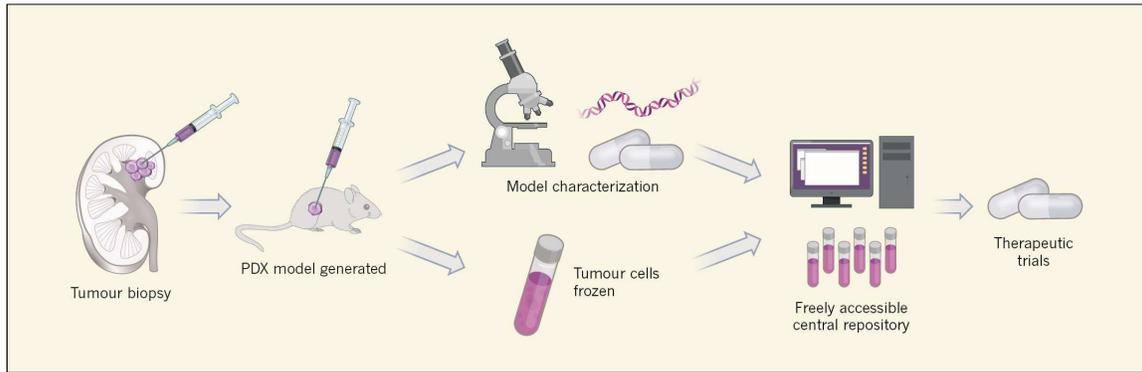
N ENGL J MED 378:20 NEJM.ORG MAY 17, 2018
The New England Journal of Medicine

Fusions may be the best targets

- Clonal
- Experience from acute leukemia
- ITK-SYK
- CTLA4-CD28
- JAK-STAT
- PDGFR

Patient-Derived Xenografts to Model Human Cancer

Murakami and Weinstock, *Nature* 2017

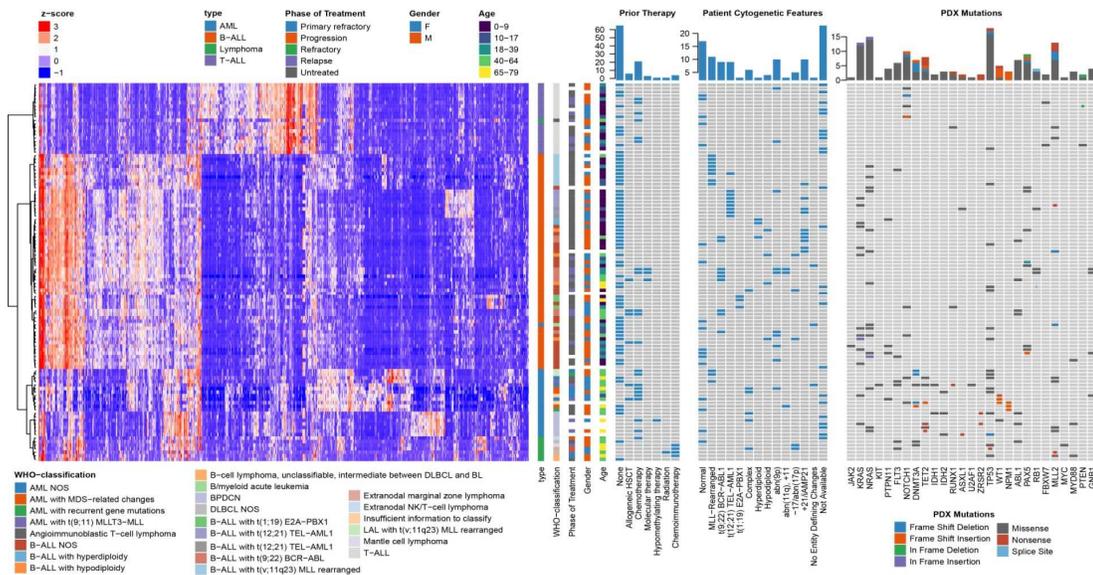


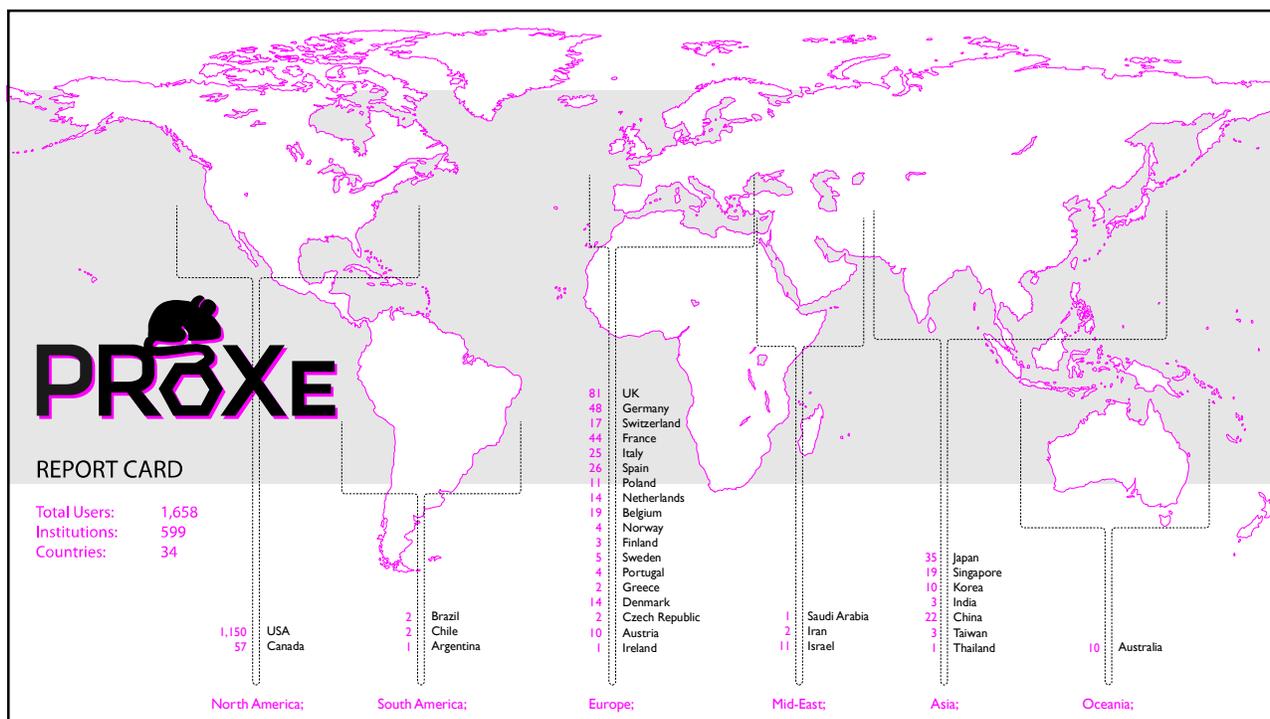
Enabling Research on Human Cancer (n~800)

Gao et al. *Nature Med* 2015; Townsend et al. *Cancer Cell* 2016, Ng et al. *Natu*

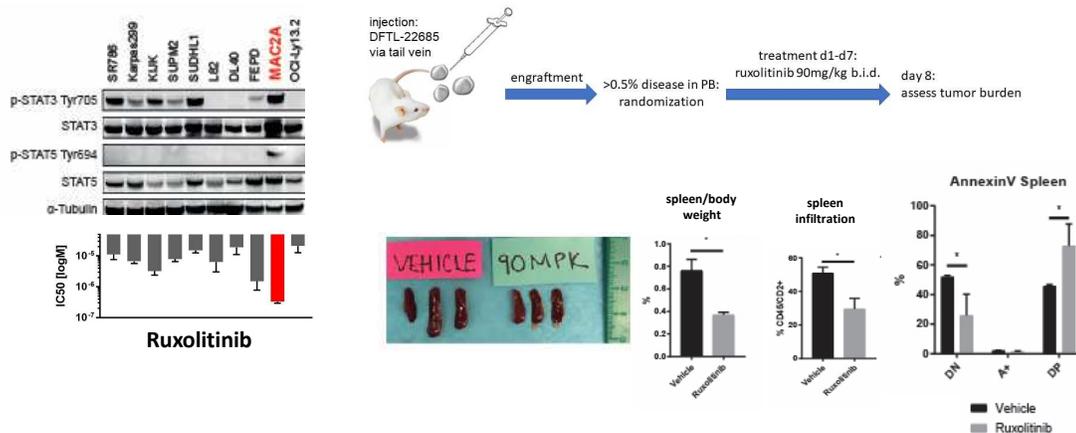
- T-ALL
 - AML
 - B-ALL
 - AUL
 - BPDCN
 - Mantle cell lymphoma
 - Double-hit lymphoma
 - Marginal zone lymphoma
 - Follicular lymphoma
 - Transformed follicular lymphoma
 - Diffuse large B-cell lymphoma
 - High-grade with MYC rearrangement
 - HSTL
 - Primary cutaneous CD30+ TCL
 - T-PLL
 - AITL
 - ALK+ ALCL
 - ALK- ALCL
 - Mycosis Fungoides
 - Sezary Syndrome
 - Extranodal NK/TCL
 - PTCL, NOS
 - ATLL
- Alveolar Soft Part Sarcoma
 - Inflammatory myofibroblastic tumor
 - Neurofibroma
 - Osteosarcoma
 - Rhabdoid tumor
 - Solid pseudopapillary tumor
 - Wilms Tumor
 - Merkel cell carcinoma
 - 400 Solid Tumors from Novartis

Now on cBioPortal

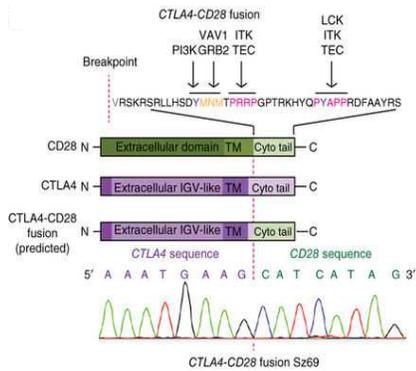




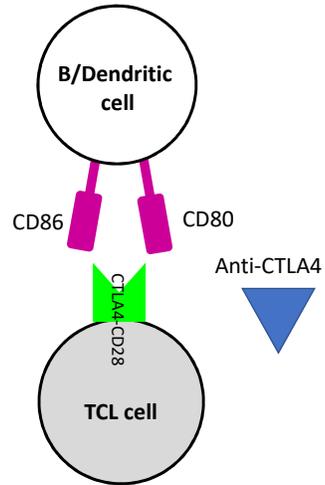
JAK2 fusion and remarkable sensitivity to ruxolitinib



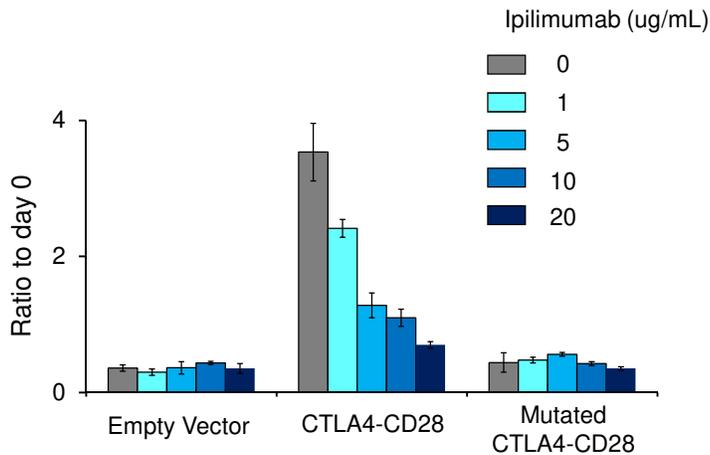
CTLA4-CD28 and ICOS-CD28 fusions co-opt checkpoint signaling



Nat Genet. 2015 47(9):1056-60



Ipilimumab blocks CTLA4-CD28-mediated transformation



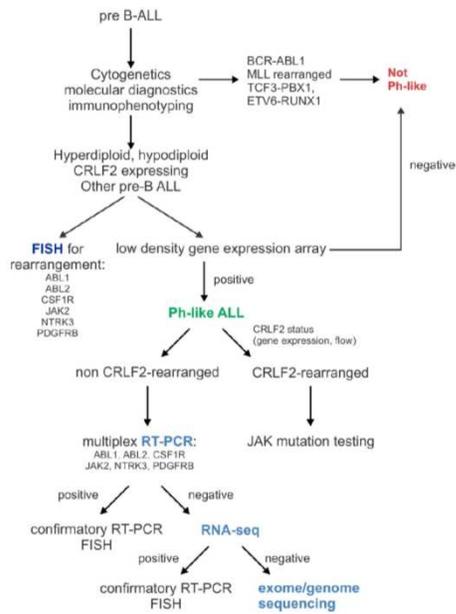
Yoshida et al. Blood 2020

PRE

POST 4 doses ipilimumab



Mol Genet Genomic Med. 2015 Mar; 3(2): 130–136

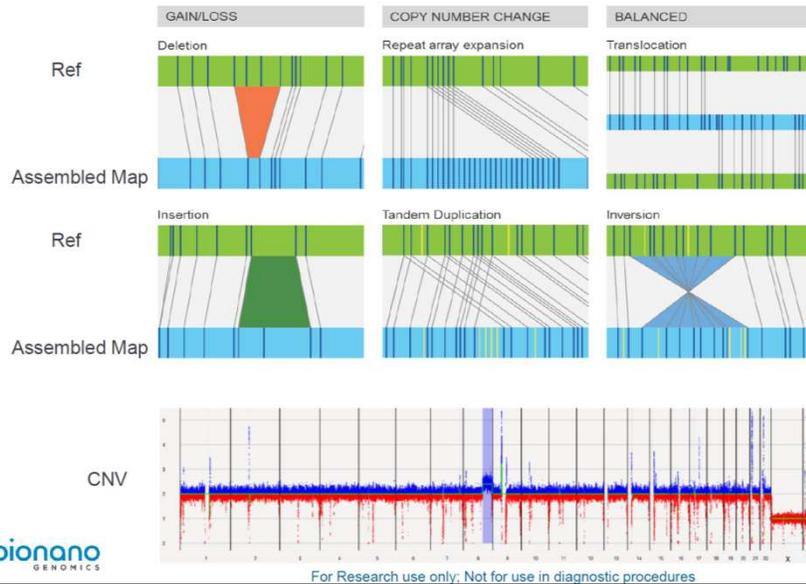


Roberts et al. NEJM 2014

Archer FusionPlex Lymphoma

KICDA	AMT3	ALK	ASB1	BATF3	BAK	BCL2	BCL2L1	BRD4	BRD9	BRG1	BRN1	BRN2	BRN3	BRN4	BRN5	BRN6	BRN7	BRN8	BRN9	BRN10	BRN11	BRN12	BRN13	BRN14	BRN15	BRN16	BRN17	BRN18	BRN19	BRN20	BRN21	BRN22	BRN23	BRN24	BRN25	BRN26	BRN27	BRN28	BRN29	BRN30	BRN31	BRN32	BRN33	BRN34	BRN35	BRN36	BRN37	BRN38	BRN39	BRN40	BRN41	BRN42	BRN43	BRN44	BRN45	BRN46	BRN47	BRN48	BRN49	BRN50	BRN51	BRN52	BRN53	BRN54	BRN55	BRN56	BRN57	BRN58	BRN59	BRN60	BRN61	BRN62	BRN63	BRN64	BRN65	BRN66	BRN67	BRN68	BRN69	BRN70	BRN71	BRN72	BRN73	BRN74	BRN75	BRN76	BRN77	BRN78	BRN79	BRN80	BRN81	BRN82	BRN83	BRN84	BRN85	BRN86	BRN87	BRN88	BRN89	BRN90	BRN91	BRN92	BRN93	BRN94	BRN95	BRN96	BRN97	BRN98	BRN99	BRN100																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																										
BCL3	BCL6	BCR	BIRC3	BLNK	BLM1	BLM2	BLM3	BLM4	BLM5	BLM6	BLM7	BLM8	BLM9	BLM10	BLM11	BLM12	BLM13	BLM14	BLM15	BLM16	BLM17	BLM18	BLM19	BLM20	BLM21	BLM22	BLM23	BLM24	BLM25	BLM26	BLM27	BLM28	BLM29	BLM30	BLM31	BLM32	BLM33	BLM34	BLM35	BLM36	BLM37	BLM38	BLM39	BLM40	BLM41	BLM42	BLM43	BLM44	BLM45	BLM46	BLM47	BLM48	BLM49	BLM50	BLM51	BLM52	BLM53	BLM54	BLM55	BLM56	BLM57	BLM58	BLM59	BLM60	BLM61	BLM62	BLM63	BLM64	BLM65	BLM66	BLM67	BLM68	BLM69	BLM70	BLM71	BLM72	BLM73	BLM74	BLM75	BLM76	BLM77	BLM78	BLM79	BLM80	BLM81	BLM82	BLM83	BLM84	BLM85	BLM86	BLM87	BLM88	BLM89	BLM90	BLM91	BLM92	BLM93	BLM94	BLM95	BLM96	BLM97	BLM98	BLM99	BLM100																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																
BTB	CARD11	CBFB	CCDC30	CCND1	CCND2	CCND3	CCND4	CCND5	CCND6	CCND7	CCND8	CCND9	CCND10	CCND11	CCND12	CCND13	CCND14	CCND15	CCND16	CCND17	CCND18	CCND19	CCND20	CCND21	CCND22	CCND23	CCND24	CCND25	CCND26	CCND27	CCND28	CCND29	CCND30	CCND31	CCND32	CCND33	CCND34	CCND35	CCND36	CCND37	CCND38	CCND39	CCND40	CCND41	CCND42	CCND43	CCND44	CCND45	CCND46	CCND47	CCND48	CCND49	CCND50	CCND51	CCND52	CCND53	CCND54	CCND55	CCND56	CCND57	CCND58	CCND59	CCND60	CCND61	CCND62	CCND63	CCND64	CCND65	CCND66	CCND67	CCND68	CCND69	CCND70	CCND71	CCND72	CCND73	CCND74	CCND75	CCND76	CCND77	CCND78	CCND79	CCND80	CCND81	CCND82	CCND83	CCND84	CCND85	CCND86	CCND87	CCND88	CCND89	CCND90	CCND91	CCND92	CCND93	CCND94	CCND95	CCND96	CCND97	CCND98	CCND99	CCND100																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																	
CD44	CD79B	CD80	CD82	CD84	CD85	CD86	CD87	CD88	CD89	CD90	CD91	CD92	CD93	CD94	CD95	CD96	CD97	CD98	CD99	CD100	CD101	CD102	CD103	CD104	CD105	CD106	CD107	CD108	CD109	CD110	CD111	CD112	CD113	CD114	CD115	CD116	CD117	CD118	CD119	CD120	CD121	CD122	CD123	CD124	CD125	CD126	CD127	CD128	CD129	CD130	CD131	CD132	CD133	CD134	CD135	CD136	CD137	CD138	CD139	CD140	CD141	CD142	CD143	CD144	CD145	CD146	CD147	CD148	CD149	CD150	CD151	CD152	CD153	CD154	CD155	CD156	CD157	CD158	CD159	CD160	CD161	CD162	CD163	CD164	CD165	CD166	CD167	CD168	CD169	CD170	CD171	CD172	CD173	CD174	CD175	CD176	CD177	CD178	CD179	CD180	CD181	CD182	CD183	CD184	CD185	CD186	CD187	CD188	CD189	CD190	CD191	CD192	CD193	CD194	CD195	CD196	CD197	CD198	CD199	CD200	CD201	CD202	CD203	CD204	CD205	CD206	CD207	CD208	CD209	CD210	CD211	CD212	CD213	CD214	CD215	CD216	CD217	CD218	CD219	CD220	CD221	CD222	CD223	CD224	CD225	CD226	CD227	CD228	CD229	CD230	CD231	CD232	CD233	CD234	CD235	CD236	CD237	CD238	CD239	CD240	CD241	CD242	CD243	CD244	CD245	CD246	CD247	CD248	CD249	CD250	CD251	CD252	CD253	CD254	CD255	CD256	CD257	CD258	CD259	CD260	CD261	CD262	CD263	CD264	CD265	CD266	CD267	CD268	CD269	CD270	CD271	CD272	CD273	CD274	CD275	CD276	CD277	CD278	CD279	CD280	CD281	CD282	CD283	CD284	CD285	CD286	CD287	CD288	CD289	CD290	CD291	CD292	CD293	CD294	CD295	CD296	CD297	CD298	CD299	CD300	CD301	CD302	CD303	CD304	CD305	CD306	CD307	CD308	CD309	CD310	CD311	CD312	CD313	CD314	CD315	CD316	CD317	CD318	CD319	CD320	CD321	CD322	CD323	CD324	CD325	CD326	CD327	CD328	CD329	CD330	CD331	CD332	CD333	CD334	CD335	CD336	CD337	CD338	CD339	CD340	CD341	CD342	CD343	CD344	CD345	CD346	CD347	CD348	CD349	CD350	CD351	CD352	CD353	CD354	CD355	CD356	CD357	CD358	CD359	CD360	CD361	CD362	CD363	CD364	CD365	CD366	CD367	CD368	CD369	CD370	CD371	CD372	CD373	CD374	CD375	CD376	CD377	CD378	CD379	CD380	CD381	CD382	CD383	CD384	CD385	CD386	CD387	CD388	CD389	CD390	CD391	CD392	CD393	CD394	CD395	CD396	CD397	CD398	CD399	CD400	CD401	CD402	CD403	CD404	CD405	CD406	CD407	CD408	CD409	CD410	CD411	CD412	CD413	CD414	CD415	CD416	CD417	CD418	CD419	CD420	CD421	CD422	CD423	CD424	CD425	CD426	CD427	CD428	CD429	CD430	CD431	CD432	CD433	CD434	CD435	CD436	CD437	CD438	CD439	CD440	CD441	CD442	CD443	CD444	CD445	CD446	CD447	CD448	CD449	CD450	CD451	CD452	CD453	CD454	CD455	CD456	CD457	CD458	CD459	CD460	CD461	CD462	CD463	CD464	CD465	CD466	CD467	CD468	CD469	CD470	CD471	CD472	CD473	CD474	CD475	CD476	CD477	CD478	CD479	CD480	CD481	CD482	CD483	CD484	CD485	CD486	CD487	CD488	CD489	CD490	CD491	CD492	CD493	CD494	CD495	CD496	CD497	CD498	CD499	CD500	CD501	CD502	CD503	CD504	CD505	CD506	CD507	CD508	CD509	CD510	CD511	CD512	CD513	CD514	CD515	CD516	CD517	CD518	CD519	CD520	CD521	CD522	CD523	CD524	CD525	CD526	CD527	CD528	CD529	CD530	CD531	CD532	CD533	CD534	CD535	CD536	CD537	CD538	CD539	CD540	CD541	CD542	CD543	CD544	CD545	CD546	CD547	CD548	CD549	CD550	CD551	CD552	CD553	CD554	CD555	CD556	CD557	CD558	CD559	CD560	CD561	CD562	CD563	CD564	CD565	CD566	CD567	CD568	CD569	CD570	CD571	CD572	CD573	CD574	CD575	CD576	CD577	CD578	CD579	CD580	CD581	CD582	CD583	CD584	CD585	CD586	CD587	CD588	CD589	CD590	CD591	CD592	CD593	CD594	CD595	CD596	CD597	CD598	CD599	CD600	CD601	CD602	CD603	CD604	CD605	CD606	CD607	CD608	CD609	CD610	CD611	CD612	CD613	CD614	CD615	CD616	CD617	CD618	CD619	CD620	CD621	CD622	CD623	CD624	CD625	CD626	CD627	CD628	CD629	CD630	CD631	CD632	CD633	CD634	CD635	CD636	CD637	CD638	CD639	CD640	CD641	CD642	CD643	CD644	CD645	CD646	CD647	CD648	CD649	CD650	CD651	CD652	CD653	CD654	CD655	CD656	CD657	CD658	CD659	CD660	CD661	CD662	CD663	CD664	CD665	CD666	CD667	CD668	CD669	CD670	CD671	CD672	CD673	CD674	CD675	CD676	CD677	CD678	CD679	CD680	CD681	CD682	CD683	CD684	CD685	CD686	CD687	CD688	CD689	CD690	CD691	CD692	CD693	CD694	CD695	CD696	CD697	CD698	CD699	CD700	CD701	CD702	CD703	CD704	CD705	CD706	CD707	CD708	CD709	CD710	CD711	CD712	CD713	CD714	CD715	CD716	CD717	CD718	CD719	CD720	CD721	CD722	CD723	CD724	CD725	CD726	CD727	CD728	CD729	CD730	CD731	CD732	CD733	CD734	CD735	CD736	CD737	CD738	CD739	CD740	CD741	CD742	CD743	CD744	CD745	CD746	CD747	CD748	CD749	CD750	CD751	CD752	CD753	CD754	CD755	CD756	CD757	CD758	CD759	CD760	CD761	CD762	CD763	CD764	CD765	CD766	CD767	CD768	CD769	CD770	CD771	CD772	CD773	CD774	CD775	CD776	CD777	CD778	CD779	CD780	CD781	CD782	CD783	CD784	CD785	CD786	CD787	CD788	CD789	CD790	CD791	CD792	CD793	CD794	CD795	CD796	CD797	CD798	CD799	CD800	CD801	CD802	CD803	CD804	CD805	CD806	CD807	CD808	CD809	CD810	CD811	CD812	CD813	CD814	CD815	CD816	CD817	CD818	CD819	CD820	CD821	CD822	CD823	CD824	CD825	CD826	CD827	CD828	CD829	CD830	CD831	CD832	CD833	CD834	CD835	CD836	CD837	CD838	CD839	CD840	CD841	CD842	CD843	CD844	CD845	CD846	CD847	CD848	CD849	CD850	CD851	CD852	CD853	CD854	CD855	CD856	CD857	CD858	CD859	CD860	CD861	CD862	CD863	CD864	CD865	CD866	CD867	CD868	CD869	CD870	CD871	CD872	CD873	CD874	CD875	CD876	CD877	CD878	CD879	CD880	CD881	CD882	CD883	CD884	CD885	CD886	CD887	CD888	CD889	CD890	CD891	CD892	CD893	CD894	CD895	CD896	CD897	CD898	CD899	CD900	CD901	CD902	CD903	CD904	CD905	CD906	CD907	CD908	CD909	CD910	CD911	CD912	CD913	CD914	CD915	CD9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CEBPD	CHIC2	CIT4	CREB1	CREB2	CREB3	CREB4	CREB5	CREB6	CREB7	CREB8	CREB9	CREB10	CREB11	CREB12	CREB13	CREB14	CREB15	CREB16	CREB17	CREB18	CREB19	CREB20	CREB21	CREB22	CREB23	CREB24	CREB25	CREB26	CREB27	CREB28	CREB29	CREB30	CREB31	CREB32	CREB33	CREB34	CREB35	CREB36	CREB37	CREB38	CREB39	CREB40	CREB41	CREB42	CREB43	CREB44	CREB45	CREB46	CREB47	CREB48	CREB49	CREB50	CREB51	CREB52	CREB53	CREB54	CREB55	CREB56	CREB57	CREB58	CREB59	CREB60</																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																										

Structural variants are called by comparing maps to a reference or to each other (Optical Genome Mapping)



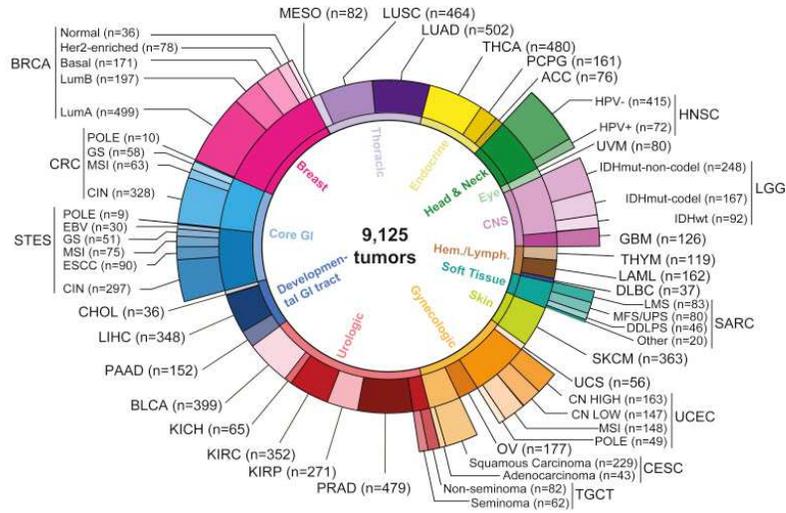
In what fraction of cases of relapsed PTCL “should” you order genetic testing?

- A None
- B 1%-25%
- C 26-75%
- D >75%
- E When is the break?

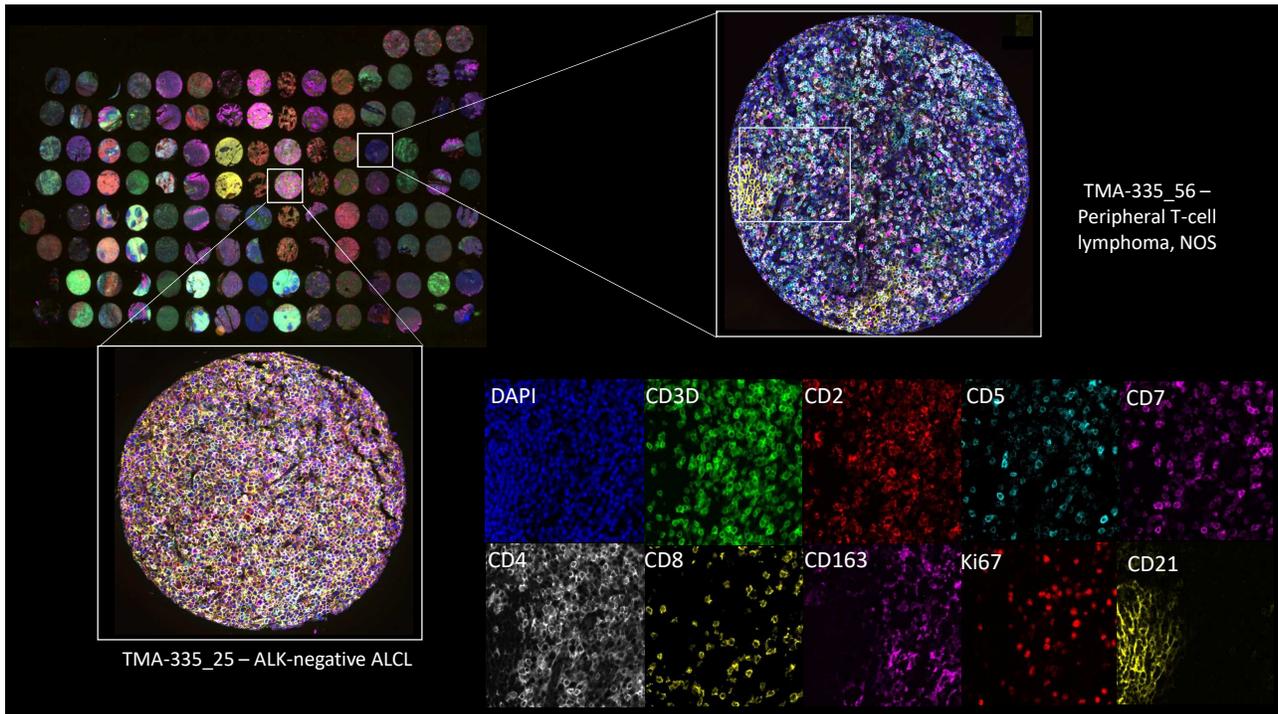
Where do we want to be in 5 years?

>500 frozen PTCLs

- Whole genome
- Exome
- Transcriptome
- Methylome
- Phosphoproteome
- Cell-free DNA



Ciriello et al., Nat Genet, 2013; Vega et al. Cell 2018



Summary

- There are limited opportunities to select therapies for R/R T-cell lymphomas based on genomics:
 - JAK fusions
 - SYK fusions
 - PDGFR fusions
 - CTLA4 fusions
 - *CD274* (PD-L1) 3' UTR alterations
- Diagnostics to identify those opportunities are imperfect but exist
- Empiricism and creativity may hurt patients
- The future is very bright