Inferring structural variant cancer cell fraction

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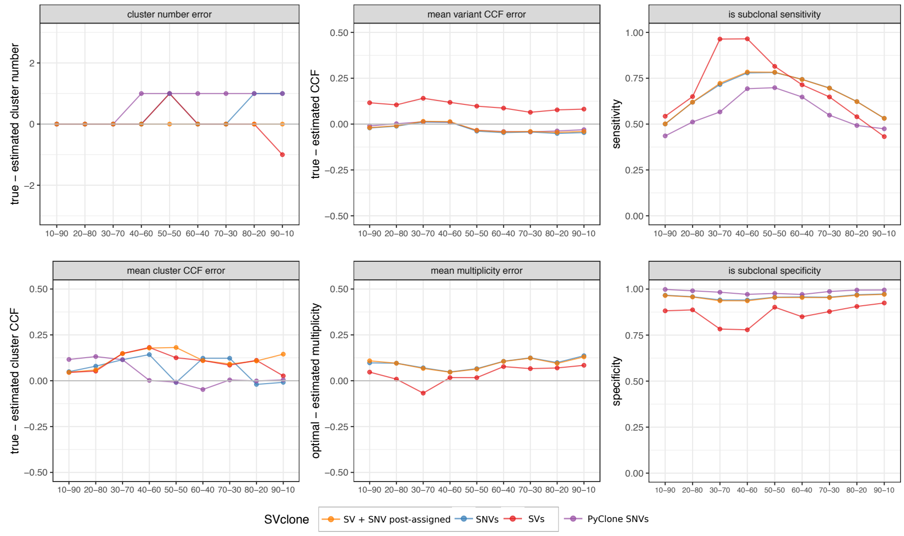
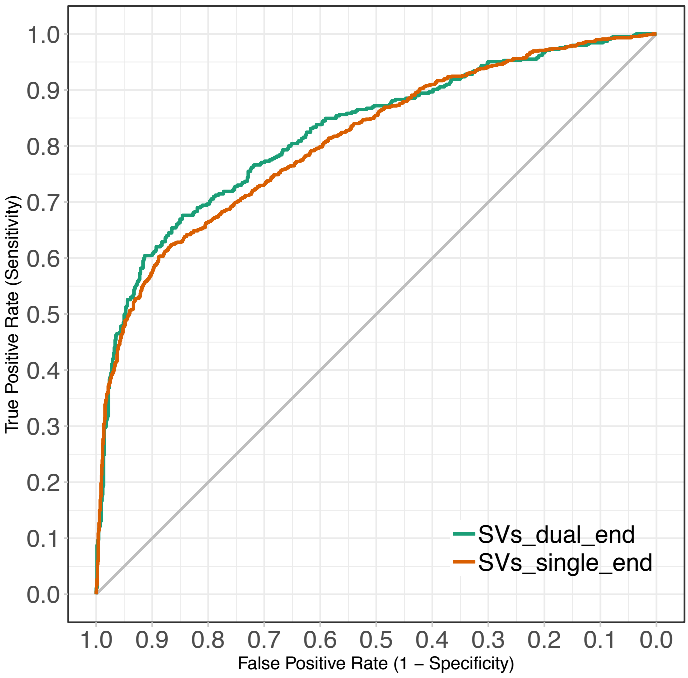
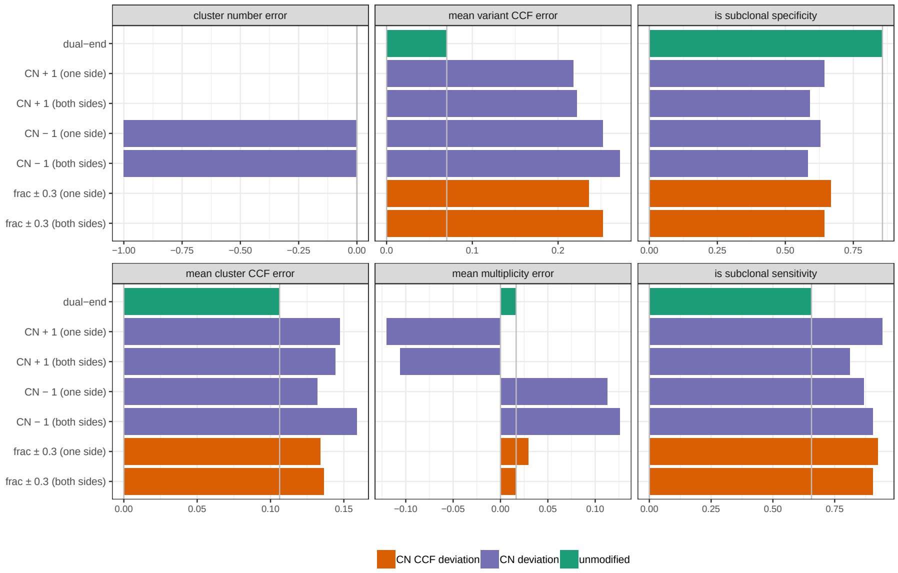
Supplementary Figures



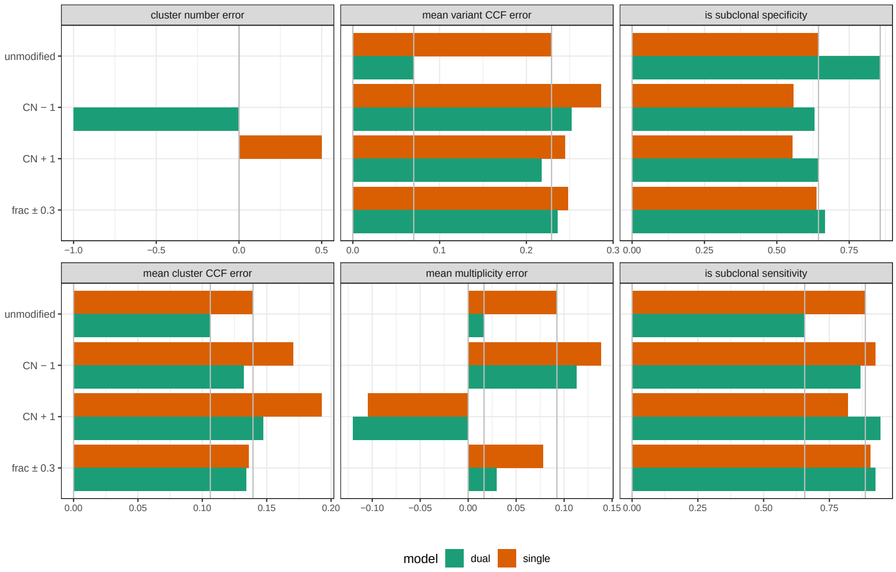
Supplementary Figure 1: Performance assessment of post assignment of variants. The first column shows the cluster number error (3 - inferred cluster number), and the mean CCF error, where true and inferred clusters are matched based on their order (see Methods). The second column shows the mean variant CCF and multiplicity error compared to the ground truth CCF. The third column shows the subclonal classification sensitivity and specificity using sample membership of the variant (i.e. a variant is classified as clonal if present in both samples of the mixture, and subclonal otherwise). Results are split into four categories: SNV and SVs post assigned by SVclone, SNVs post assigned by SVclone, SVs post assigned by SVclone, and SNVs post-assigned by Pyclone. Post assigning SVs and SNVs to a joint model yields improvements in mean variant CCF, multiplicity error and subclonal classification sensitivity and specificity. Utilising both SNV and SV data, the correct cluster number is inferred for the 50-50 mix.



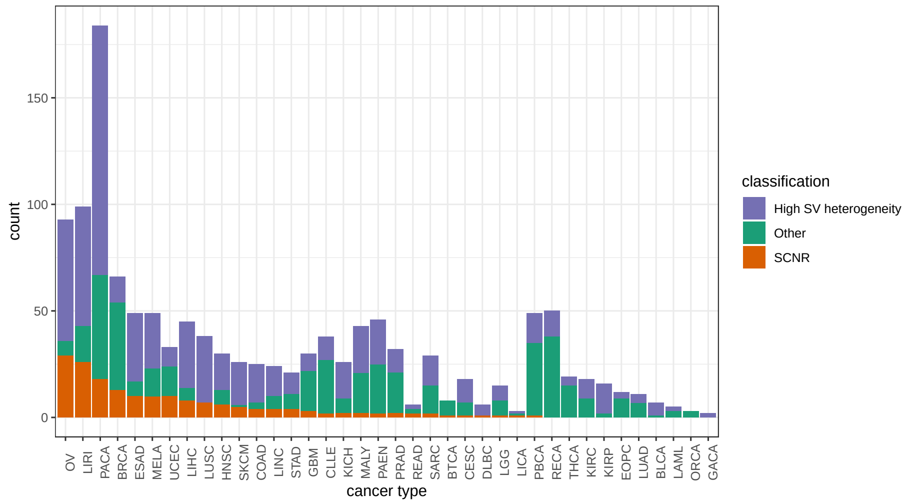
Supplementary Figure 2: Performance of subclonal classification of variants. The ROC curves shows classification of an SV as subclonal or clonal for the dual-end and single-end models, using the 3-cluster *in silico* mixture data. The respective AUCs for the dual and single-end models are 0.8234 and 0.8095.



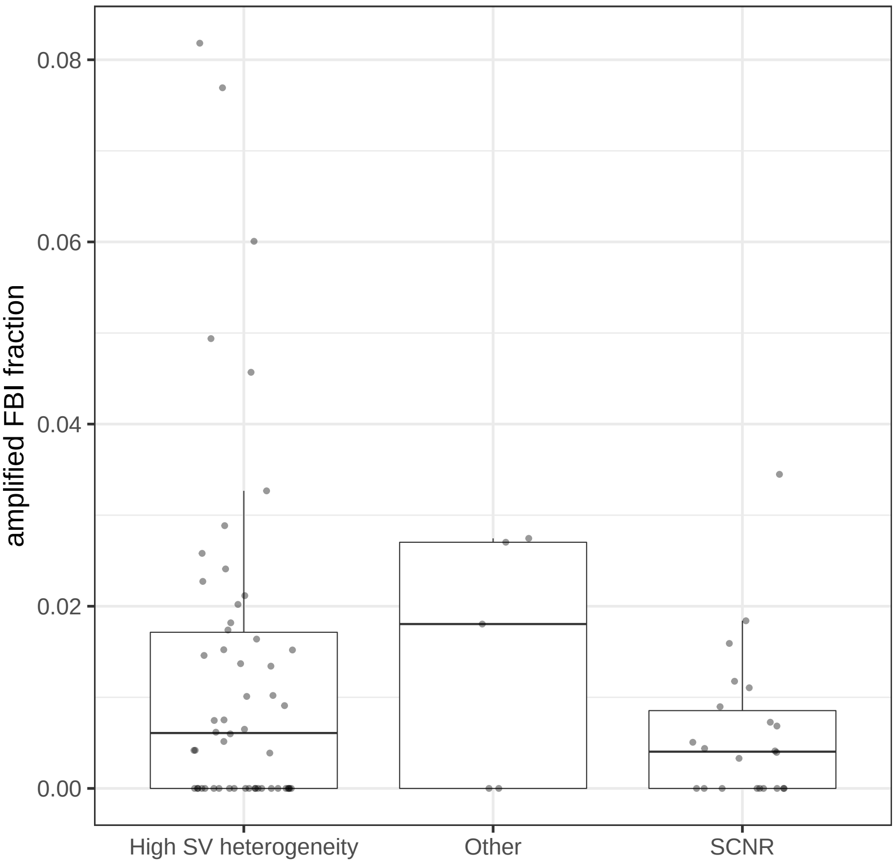
Supplementary Figure 3: Assessment of the effect of background copy-number perturbation. Comparison of clustering metrics in the unmodified dual-end model under various background copy-number perturbations (+1 and -1 from major allele copy-number, and +0.3 or -0.3 from the copy-number fraction for subclonal copy-numbers). Metrics for cluster number error, mean cluster CCF error and mean variant CCF error are all measured as the true minus estimated value. Multiplicity error is measured as the 'optimal' minus estimated value.



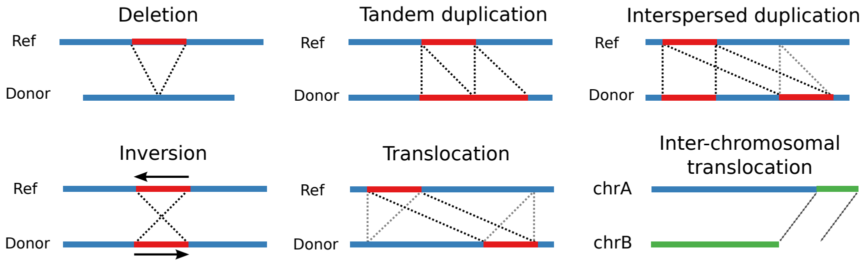
Supplementary Figure 4: Assessment of the effect of copy-number perturbations on the dual versus single-end models. Metrics for the single-end model are averaged across runs from the l and u sides (which were run separately). The dual-end model perturbations were perturbed on the l side only. Metrics are the described in Supplementary Figure 3.



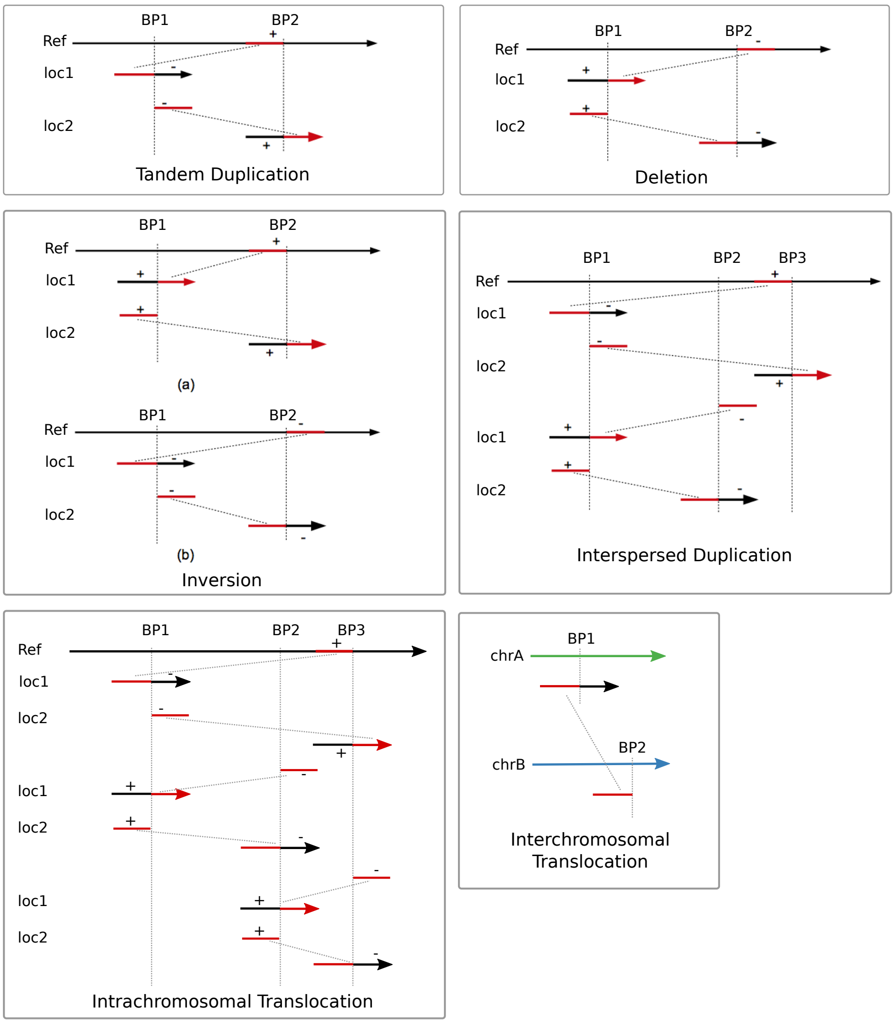
Supplementary Figure 5: Number of samples per histotype classified as SCNR, high fraction of SV subclonality, or other.



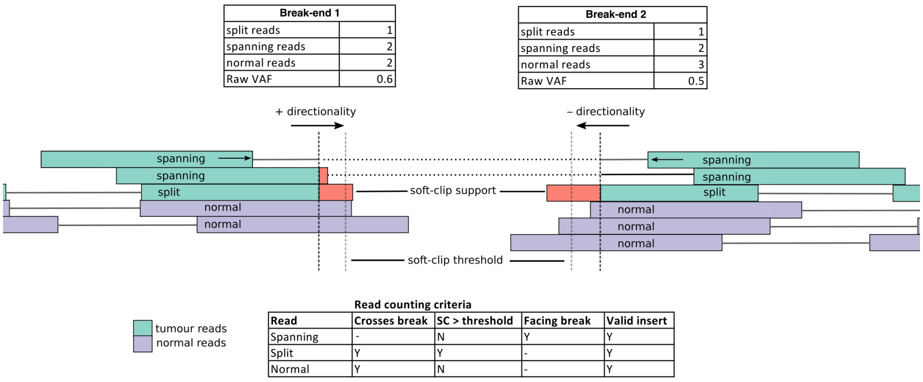
Supplementary Figure 6: Fold-back inversion (FBI) fraction for high-SV heterogeneity, other and SCNR phenotypes. No correlation between FBI and the SCNR phenotype is apparent.



Supplementary Figure 7: A schematic of the classes of structural variation identified by SVclone. Ref denotes the reference genome and donor to the modified genome.



Supplementary Figure 8: SV patterns used by SVclone to classify SV events. SVs are classified from one or more breakpoints that are part of the same SV event. Tandem duplications and deletions consist of one breakpoint, where the directionality of $(-, +)$ (where $-$ indicates that the break occurs on the left side, and $+$ the right) for duplications and $(+, -)$ for deletions. Inversions consist of two breakpoints with $(+, +)$ and $(-, -)$ directionality. Interspersed duplications consist of two breakpoints and 3 break-points with a duplication pattern at breakpoints BP1 and BP3, and a deletion pattern at breakpoints BP1 and BP2. Intra-chromosomal translocations consist of 3 breakpoints consisting of an interspersed duplication pattern, in addition to a deletion at BP2 and BP3. We consider any breakpoints where BP1 and BP2 lie on different chromosomes to be inter-chromosomal translocations.



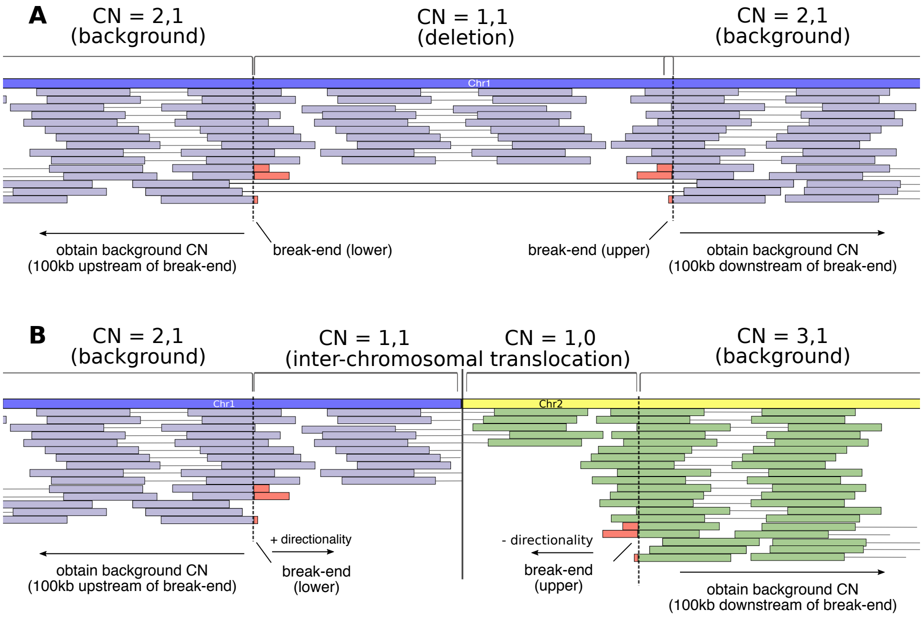
Break-end 1	
split reads	1
spanning reads	2
normal reads	2
Raw VAF	0.6

Break-end 2	
split reads	1
spanning reads	2
normal reads	3
Raw VAF	0.5

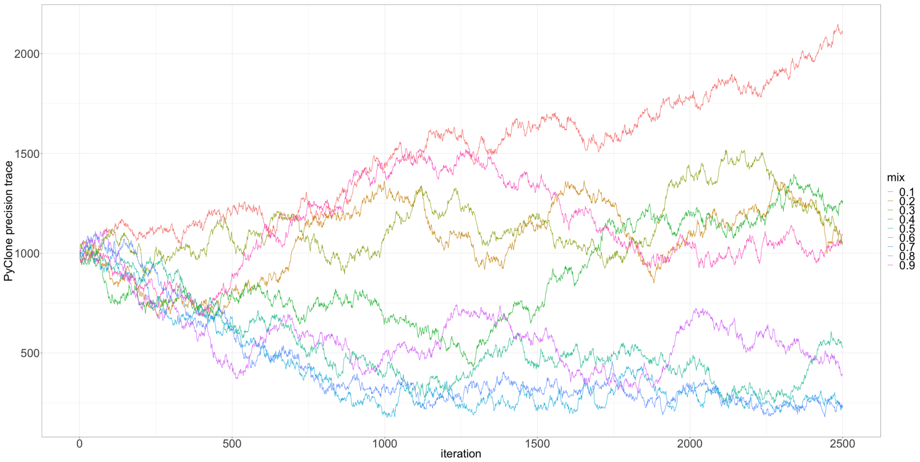
Read counting criteria

Read	Crosses break	SC > threshold	Facing break	Valid insert
Spanning	-	N	Y	Y
Split	Y	Y	-	Y
Normal	Y	N	-	Y

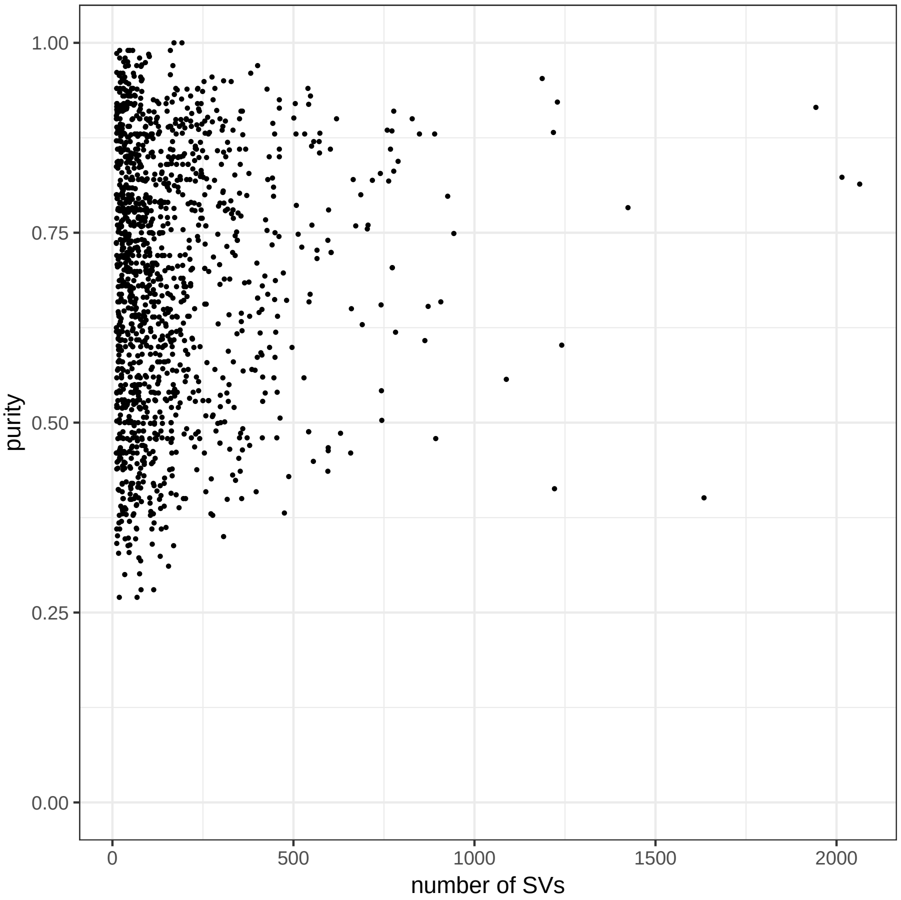
Supplementary Figure 9: Schematic showing how reads align across SV breakpoints. Reads crossing SV break-end loci are counted as supporting split reads, supporting spanning reads, normal reads or are skipped and considered anomalous. All supporting and normal reads must have a valid insert size. Insert sizes for discordant/spanning reads are calculated as the summed distance to each break-end. Split reads must be soft-clipped above the soft-clip threshold and cross the break. Normal reads must cross the break but not be soft-clipped. Spanning reads must also be oriented towards each break-end. Reads crossing the break but failing to pass the supporting or normal criteria are considered anomalous.



Supplementary Figure 10: Schematic showing an example for how background copy numbers are inferred for (**A**) intra-chromosomal variants (upstream of the lower SV break-end and downstream of the upper SV breakpoint), and (**B**) inter-chromosomal translocations (upstream for + directionality break-ends and upstream for − directionality break-ends).



Supplementary Figure 11: PyClone precision traces for the three-cluster *in silico* mixtures. The large variance of the trace values and lack of clear convergence shows the difficulty of estimating dispersion in moderate coverage ($\tilde{6}$0x) and purity ($\tilde{5}$0%) data.



Supplementary Figure 12: Number of SVs versus purity for 2436 PCAWG samples with > 0 SVs, showing that SV number is uncorrelated with purity ($R^2 = 0.0001$).

1 Supplementary Tables

Supplementary Table 1: PCAWG SV vs. SNV statistics per histology group. High SV heterogeneity is defined as > 50% subclonal SVs. SVs with different background copy-number states at their two ends are considered to have heterogeneous CN states. Mean and median values were calculated across the whole cohort.

Histology abbreviation	Samples	High SV het. (samp.)	High SV het. (prop.)	Median Het. CN fraction	Mean # of SVs	Mean # of SNVs
Lung-SCC	37	37	1	0.65	176	46045
Ovary-AdenoCA	93	86	0.92	0.52	217	8674
ColoRect-AdenoCA	26	24	0.92	0.49	63	112812
Liver-HCC	156	133	0.85	0.5	76	13243
Eso-AdenoCA	48	41	0.85	0.62	204	32317
Skin-Melanoma	75	61	0.81	0.58	149	107468
Bone-Osteosarc	18	14	0.78	0.75	234	5878
Panc-AdenoCA	179	132	0.74	0.61	84	6820
Lymph-BNHL	26	19	0.73	0.35	55	15163
Head-SCC	33	23	0.7	0.48	92	18407
Stomach-AdenoCA	23	16	0.7	0.42	129	19605
Uterus-AdenoCA	26	17	0.65	0.55	172	10043
CNS-Medullo	17	10	0.59	0.61	26	1836
Panc-Endocrine	21	12	0.57	0.38	40	4234
Breast-AdenoCA	98	40	0.41	0.61	242	7108
Prost-AdenoCA	123	48	0.39	0.4	93	3576
CNS-GBM	29	11	0.38	0.57	93	15293
Lung-AdenoCA	11	4	0.36	0.56	104	28624
Kidney-RCC.clearcell	33	8	0.24	0.55	57	7223
Biliary-AdenoCA	13	3	0.23	0.64	84	24829
TOTAL	1085	739	0.68			
MEAN				0.52	125	20956
MEDIAN				0.53	76	7425

Supplementary Table 2: SCNR SV clustering and linkage statistics vs. non-SCNR, non-SV-enriched cohort.

	SCNR	**Other**
Clustered SVs (all)	0.9704	0.8712
Clonal clustered SVs	0.2694	0.1649
Subclonal clustered SVs	0.3911	0.3132
Chromosomes walkable	0.02734	0.0209
Samples with clustered SVs linked by INTRXs	0.5031	0.2159

Supplementary Table 3: Variants involved in candidate bi-allelic hits of driver genes in the high SV heterogeneity (HSVH) and subclonal neutral rearrangement (SCNR) cohorts. Percentages indicate fraction of cohort affected by at least one such event ($N = 650$ for HSVH and $N = 177$ for SCNR). Hits columns indicate the number of clonal and subclonal genes affected per cohort by the variant type.

Variant	**Cohort**	**Samples affected by clonal var**	**Samples affected by subcl. var**	**Clonal hits**	**Subcl. hits**
Balanced SV	HSVH	280 (43.08%)	209 (32.15%)	554	344
Unbalanced SV	HSVH	377 (58%)	243 (37.38%)	963	487
SNV/INDEL	HSVH	511 (78.62%)	100 (15.38%)	1084	124
(clonal) LoH	HSVH	634 (97.54%)	–	86535	–
Balanced SV	SCNR	118 (66.67%)	110 (62.15%)	318	238
Unbalanced SV	SCNR	156 (88.14%)	97 (54.8%)	773	242
SNV/INDEL	SCNR	138 (77.97%)	18 (10.17%)	275	20
(clonal) LoH	SCNR	177 (100%)	–	28067	–

Supplementary Table 4: Directionality assignment summary. # SV pairs is the total number of SV breakpoints with matching loci, # matching is the number of loci (of 2) per break-end that match. Ranks considers how the SV breakpoints rank against each other by locus on the same chromosome. SV1-3 show the outcome assignments. D indicates the original break-end direction; * indicates a new SV breakpoint is created.

		# Matching				
# Mixed	# SV pairs	# matching break-ends	Break-end ranks	SV1	SV2	SV3
1	–	–	–	$(D,-)$	$(D,+)^*$	–
2	1	0	–	$(-,-)$	$(+,+)^*$	–
2	2	2	–	$(-,-)$	$(+,+)$	–
2	3	1	$[(1,2),(2,3),(1,3)]$	$(+,-)$	$(+,-)$	$(-,+)$

Supplementary Table 5: SV offsets for matching SCNA states to SV loci. l and u represent two break-ends of a breakpoint, where $l < u$ (intra-chromosomal rearrangements, in inter-chromosomal rearrangements l is break-end of the lower chromosome) and dir_l and dir_u representing the directionality of each respective break-end ($dir_x \in \{+,-\}$); f is a pre-specified offset (100kb by default).

Translocation type	l offset	u offset
inter-chromosomal	$l-(dir_l \cdot f)$	$u-(dir_u \cdot f)$
intra-chromosomal	$l-f$	$u+f$

Supplementary Table 6: Fraction of SVs where background copy-numbers vary between ends in 001bM, 001gM and all 3-cluster mixtures.

Mixture	**CN heterogeneity**
001bM	0.31
001gM	0.38
10-90	0.26
20-80	0.25
30-70	0.27
40-60	0.25
50-50	0.25
60-40	0.24
70-30	0.24
80-20	0.25
90-10	0.25

2 Supplementary Notes

Supplementary Note 1

SVclone was run on the following PCAWG samples (all these samples were multi-sample representative and had a number of reads per chromosome copy of at least 10):

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Supplementary Note 2

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Patterns of structural variations, signatures, genomic correlations, retrotransposons, mobile elements

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Germline cancer genome

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Evolution and heterogeneity

David J Adams[1], Pavana Anur[375], Rameen Beroukhim[3,6,171], Paul C Boutros[9,130,139,140], David D L Bowtell[187,290], Peter J Campbell[1,2], Shaolong Cao[145], Elizabeth L Christie[187], Yupeng Cun[379], Kevin J Dawson[1], Jonas Demeulemeester[63,64], Stefan C Dentro[1,64,356], Amit G Deshwar[380], Nilgun Donmez[148,156], Ruben M Drews[293], Roland Eils[52,54,66,67], Yu Fan[145], Matthew W Fittall[64], Dale W Garsed[187,188], Moritz Gerstung[7,8], Gad Getz[3,4,5,6], Santiago Gonzalez[7,8], Gavin Ha[3], Kerstin Haase[64], Marcin Imielinski[298,299], Lara Jerman[8,381], Yuan Ji[382,383], Clemency Jolly[64], Kortine Kleinheinz[52,54], Juhee Lee[384], Henry Lee-Six[1], Ignaty Leshchiner[3], Dimitri Livitz[3], Salem Malikic[148,156], Iñigo Martincorena[1], Thomas J Mitchell[1,294,385], Quaid D Morris[360,386], Ville Mustonen[319,320,321], Layla Oesper[387], Martin Peifer[379], Myron Peto[388], Benjamin J Raphael[209], Daniel Rosebrock[3], Yulia Rubanova[157,360], S Cenk Sahinalp[148,155,156], Adriana Salcedo[9], Matthias Schlesner[52,108], Steven E Schumacher[3,216], Subhajit Sengupta[389], Ruian Shi[386], Seung Jun Shin[264], **Paul T Spellman#**[390], Oliver Spiro[3], Lincoln D Stein[9,10], Maxime Tarabichi[1,64], **Peter Van Loo#**[63,64], Shankar Vembu[386,391], Ignacio Vázquez-García[1,164,327,328], Wenyi Wang[145], **David C Wedge#**[1,356,357], David A Wheeler[161,162], Jeffrey A Wintersinger[190,360,392], Tsun-Po Yang[379], Xiaotong Yao[298,315], Kaixian Yu[393], and Hongtu Zhu[394,395]

Exploratory: portals, visualization and software infrastructure

Fatima Al-Shahrour[359], Elisabet Barrera[7], Wojciech Bazant[7], Alvis Brazma[7], Isidro Cortés-Ciriano[236,237,238], Brian Craft[239], David Craft[3,240], Vincent Ferretti[45,68], Nuno A Fonseca[7,69], Anja Füllgrabe[7], Mary J Goldman[239], **David Haussler#**[239,396], Wolfgang Huber[8], Maria Keays[7], Alfonso Muñoz[7], Brian D O'Connor[45,50], Irene Papatheodorou[7], Robert Petryszak[7], Elena Piñeiro-Yáñez[359], Alfonso Valencia[46,109], **Miguel Vazquez#**[46,110], John N Weinstein[397,398], Qian Xiang[114], Junjun Zhang[45] and **Jingchun Zhu#**[239]

Exploratory: mitochondrial variants and HLA/immunogenicity

Peter J Campbell[1,2], Yiwen Chen[145], Chad J Creighton[241], Li Ding[135,136,143], Akihiro Fujimoto[48], Masashi Fujita[48], Gad Getz[3,4,5,6], Leng Han[230], Takanori Hasegawa[86], Shuto Hayashi[86], Seiya Imoto[85,86], Young Seok Ju[1,181], Hyung-Lae Kim[27], Youngwook Kim[95,96], Youngil Koh[306,307], Mitsuhiro Komura[86], Jun Li[145], **Han Liang#**[399], Iñigo Martincorena[1], Satoru Miyano[86], Shinichi Mizuno[400], **Hidewaki Nakagawa#**[48], Keunchil Park[205,206], Eigo Shimizu[86], Yumeng Wang[145,401], John N Weinstein[397,398], Yanxun Xu[402], Rui Yamaguchi[86], Fan Yang[386], Yang Yang[230], Christopher J Yoon[181], Sung-Soo Yoon[307], Yuan Yuan[145], Fan Zhang[246] and Zemin Zhang[246,271]

Exploratory: pathogens

Malik Alawi[403,404], Ivan Borozan[9], Daniel S Brewer[405,406], Colin S Cooper[406,407,408], Nikita Desai[45], **Roland Eils#**[52,54,66,67], Vincent Ferretti[45,68], Adam Grundhoff[403,409], Murat Iskar[410], Kortine Kleinheinz[52,54], **Peter Lichter#**[79,410], Hidewaki Nakagawa[48], Akinyemi I Ojesina[255,256,257], Chandra Sekhar Pedamallu[3,6,171], Matthias Schlesner[52,108], Xiaoping Su[141] and Marc Zapatka[410]

Tumor Specific Providers – Australia (Ovarian cancer)

Kathryn Alsop[411,412], Australian Ovarian Cancer Study Group[187,310,413], **David D L Bowtell#**[187,290], Timothy JC Bruxner[185], Angelika N Christ[185], Elizabeth L Christie[187], Stephen M Cordner[414], Prue A Cowin[187], Ronny Drapkin[415], Dariush Etemadmoghadam[187,188], Sian Fereday[416], Dale W Garsed[187,188], Joshy George[167], Sean M Grimmond[365], Anne Hamilton[187], Oliver Holmes[310,311], Jillian A Hung[417,418], Karin S Kassahn[185,419], Stephen H Kazakoff[310,311], Catherine J Kennedy[420,421], Conrad R Leonard[310,311], Linda Mileshkin[187], David K Miller[185,362,422], Gisela Mir Arnau[187], Chris Mitchell[187], Felicity Newell[310,311], Katia Nones[310,311], Ann-Marie Patch[310,311], John V Pearson[310,311], Michael C Quinn[310,311], Mark Shackleton[188,217], Darrin F Taylor[185], Heather Thorne[187], Nadia Traficante[187], Ravikiran Vedururu[187], Nick M Waddell[311], Nicola Waddell[310,311], Paul M Waring[253], Scott Wood[310,311], Qinying Xu[310,311] and Anna deFazio[423,424,425]

Tumor Specific Providers – Australia (Pancreatic cancer)

Matthew J Anderson[185], Davide Antonello[426], Andrew P Barbour[427,428], Claudio Bassi[426], Samantha Bersani[429], **Andrew V Biankin#**[361,362,363,364], Timothy JC Bruxner[185], Ivana Cataldo[429,430], David K Chang[362,364], Lorraine A Chantrill[362], Yoke-Eng Chiew[423], Angela Chou[362,431], Angelika N Christ[185], Sara Cingarlini[37], Nicole Cloonan[432], Vincenzo Corbo[430,433, 434], Fraser R Duthie[435,436], J Lynn Fink[46,185], Anthony J Gill[362,437], Janet S Graham[364,438], **Sean M Grimmond#**[365], Ivon Harliwong[185], Oliver Holmes[310,311], Nigel B Jamieson[363,364,439], Amber L Johns[362,422], Karin S Kassahn[185,419], Stephen H Kazakoff[310,311], James G Kench[362,437,440], Luca Landoni[426], Rita T Lawlor[430], Conrad R Leonard[310,311], Andrea Mafficini[430], Neil D Merrett[426,441], David K Miller[185,362,422], Marco Miotto[426], Elizabeth A Musgrove[364], Adnan M Nagrial[362], Felicity Newell[310,311], Katia Nones[310,311], Karin A Oien[253,442], Marina Pajic[362], Ann-Marie Patch[310,311], John V Pearson[310,311], Mark Pinese[362], Andreia V Pinho[362], Michael C Quinn[310,311], Alan J Robertson[185], Ilse Rooman[362], Borislav C Rusev[430], Jaswinder S Samra[426,437], Maria Scardoni[429], Christopher J Scarlett[362,443], Aldo Scarpa[430], Elisabetta Sereni[426], Katarzyna O Sikora[430], Michele Simbolo[433], Morgan L Taschuk[45], Christopher W Toon[362], Giampaolo Tortora[37,38], Caterina Vicentini[430], Nick M Waddell[311], Nicola Waddell[310,311], Scott Wood[310,311], Jianmin Wu[362], Qinying Xu[310,311] and Nikolajs Zeps[444]

Tumor Specific Providers – Australia (Skin cancer)

Lauri A Aaltonen[445], Andreas Behren[446], Hazel Burke[447], Jonathan Cebon[446], Rebecca A Dagg[448], Ricardo De Paoli-Iseppi[449], Ken Dutton-Regester[310], Matthew A Field[450], Anna Fitzgerald[451], Sean M Grimmond[365], **Nicholas K Hayward#**[310,447], Peter Hersey[447], Oliver Holmes[310,311], Valerie Jakrot[447], Peter A Johansson[310], Hojabr Kakavand[449], Stephen H Kazakoff[310,311], Richard F Kefford[452], Loretta MS Lau[453], Conrad R Leonard[310,311], Georgina V Long[454], **Graham J Mann#**[455,456], Felicity Newell[310,311], Katia Nones[310,311], Ann-Marie Patch[310,311], John V Pearson[310,311], Hilda A Pickett[453], Antonia L Pritchard[310], Gulietta M Pupo[457], Robyn PM Saw[454], Sarah-Jane Schramm[458], **Richard A Scolyer#**[424,454,459,460], Mark Shackleton[188,217], Catherine A Shang[461], Ping Shang[454], Andrew J Spillane[454], Jonathan R Stretch[454], Varsha Tembe[458], John F Thompson[454], Ricardo E Vilain[459], Nick M Waddell[311], Nicola Waddell[310,311], James S Wilmott[454], Scott Wood[310,311], Qinying Xu[310,311] and Jean Y Yang[462]

Tumor Specific Providers – Canada (Pancreatic cancer)

John Bartlett[463,464], Prashant Bavi[465], Ivan Borozan[9], Dianne E Chadwick[466], Michelle Chan-Seng-Yue[465], Sean Cleary[465,467], Ashton A Connor[468,469], Karolina Czajka[470], Robert E Denroche[465], Neesha C Dhani[471], Jenna Eagles[78], Vincent Ferretti[45,68], Steven Gallinger[465,468,469], Robert C Grant[465,472], David Hedley[471], Michael A Hollingsworth[473], **Thomas J Hudson#**[77,78], Gun Ho Jang[465], Jeremy Johns[78], Sangeetha Kalimuthu[465], Sheng-Ben Liang[474], Ilinca Lungu[465,475], Xuemei Luo[9], Faridah Mbabaali[78], **John D McPherson#**[78,465,476], Treasa A McPherson[472], Jessica K Miller[78], Malcolm J Moore[471], Faiyaz Notta[465,477], Danielle Pasternack[78], Gloria M Petersen[478], Michael H A Roehrl[130,465,479,480,481], Michelle Sam[78], Iris Selander[472], Stefano Serra[253], Sagedeh Shahabi[474], **Lincoln D Stein#**[9,10], Morgan L Taschuk[45], Sarah P Thayer[104], Lee E Timms[78], Gavin W Wilson[9,465], Julie M Wilson[465] and Bradly G Wouters[482]

Tumor Specific Providers – Canada (Prostate cancer)

Timothy A Beck[45], Vinayak Bhandari[9], Paul C Boutros[9,130,139,140], **Robert G Bristow#**[130,483,484,485,486], Colin C Collins[148], Shadrielle MG Espiritu[9], Neil E Fleshner[487], Natalie S Fox[9], Michael Fraser[9], Syed Haider[9], Lawrence E Heisler[488], Vincent Huang[9], Emilie Lalonde[9], Julie Livingstone[9], John D McPherson[78,465,476], Alice Meng[489], Veronica Y Sabelnykova[9], Adriana Salcedo[9], Yu-Jia Shiah[9], Theodorus Van der Kwast[490] and Takafumi N Yamaguchi[9]

Tumor Specific Providers – China (Gastric cancer)

Shuai Ding[491], Daiming Fan[492], Yong Hou[39,249], Yi Huang[150,151], Lin Li[39], Siliang Li[39,249], Dongbing Liu[39,249], Xingmin Liu[39,249], **Youyong Lu#**[28,29,30], Yongzhan Nie[492,493], Hong Su[39,249], Jian Wang[39], Kui Wu[39,249], Xiao Xiao[151], Rui Xing[29,494], **Huanming Yang#**[39], Shanlin Yang[491], Yingyan Yu[495, 229], Xiuqing Zhang[39], Yong Zhou[39] and Shida Zhu[39,249]

Tumor Specific Providers – EU: France (Renal cancer)

Rosamonde E Banks[496], Guillaume Bourque[497,498], Alvis Brazma[7], Paul Brennan[499], **Mark Lathrop#**[498], Louis Letourneau[500], Yasser Riazalhosseini[498], Ghislaine Scelo[499], **Jörg Tost#**[501], Naveen Vasudev[502] and Juris Viksna[503]

Tumor Specific Providers – EU: United Kingdom (Breast cancer)

Sung-Min Ahn[504], Ludmil B Alexandrov[1,316], Samuel Aparicio[505], Laurent Arnould[506], MR Aure[507], Shriram G Bhosle[1], E Birney[7], Ake Borg[508], S Boyault[509], AB Brinkman[510], JE Brock[511], A Broeks[512], Adam P Butler[1], AL Børresen-Dale[507], C Caldas[513,514], Peter J Campbell[1,2], Suet-Feung Chin[513,514], Helen Davies[1], C Desmedt[515], L Dirix[516], S Dronov[1], Anna Ehinger[517], JE Eyfjord[518], GG Van den Eynden[519], A Fatima[216], Jorge Reis Filho[520], JA Foekens[521], PA Futreal[522], Øystein Garred[523,524], Moritz Gerstung[7,8], Dilip D Giri[520], D Glodzik[1], Dorthe Grabau[525], Holmfridur Hilmarsdottir[518], GK Hooijer[526], Jocelyne Jacquemier[527], SJ Jang[528], Jon G Jonasson[518], Jos Jonkers[529], HY Kim[527], Tari A King[530,531], Stian Knappskog[1], G Kong[527], S Krishnamurthy[532], S Van Laere[516], SR

Lakhani[533], A Langerød[507], Denis Larsimont[534], HJ Lee[528], JY Lee[535], Ming Ta Michael Lee[522], Yilong Li[1], Ole Christian Lingjærde[536], Gaetan MacGrogan[537], JW Martens[538], Sancha Martin[1,371], Iñigo Martincorena[1], Andrew Menzies[1], Sandro Morganella[1], Ville Mustonen[319,320,321], Serena Nik-Zainal[1,323,324,325], Sarah O'Meara[1], I Pauporté[18], Sarah Pinder[539], X Pivot[540], Elena Provenzano[541], CA Purdie[542], Keiran M Raine[1], M Ramakrishna[1], K Ramakrishnan[1], AL Richardson[216], M Ringnér[508], Javier Bartolomé Rodriguez[46], FG Rodríguez-González[174], G Romieu[543], Roberto Salgado[253], Torill Sauer[536], R Shepherd[1], AM Sieuwerts[177], PT Simpson[533], M Smid[544], C Sotiriou[55], PN Span[545], J Staaf[508], Lucy Stebbings[1], Ólafur Andri Stefánsson[546], Alasdair Stenhouse[547], **Michael Rudolf Stratton#**[1], HG Stunnenberg[249,548], Fred Sweep[549], BK Tan[550], Jon W Teague[1], Gilles Thomas[551], AM Thompson[547], S Tommasi[552], I Treilleux[553,554], Andrew Tutt[216], NT Ueno[395], Peter Van Loo[63,64], P Vermeulen[516], Alain Viari[430], MJ van de Vijver[253], A Vincent-Salomon[548], David C Wedge[1,356,357], Bernice Huimin Wong[555], Lucy Yates[1], X Zou[1], CHM van Deurzen[538] and L van't Veer[556,557]

Tumor Specific Providers – Germany (Malignant lymphoma)

Ole Ammerpohl[558,559], Sietse Aukema[560,561], Anke K Bergmann[562], Stephan H Bernhart[276,277,280], Hans Binder[276,277], Arndt Borkhardt[563], Christoph Borst[564], Benedikt Brors[81,117,278], Birgit Burkhardt[565], Alexander Claviez[566], Roland Eils[52,54,66,67], Maria Elisabeth Goebler[567], Andrea Haake[558], Siegfried Haas[564], Martin Hansmann[568], Jessica I Hoell[563], Steve Hoffmann[276,277,279,280], Michael Hummel[569], Daniel Hübschmann[54,66,82,83,84], Dennis Karsch[570], Wolfram Klapper[561], Kortine Kleinheinz[52,54], Michael Kneba[570], Jan O Korbel[7,8], Helene Kretzmer[277,280], Markus Kreuz[571], Dieter Kube[572], Ralf Küppers[573], Chris Lawerenz[67], Dido Lenze[569], Peter Lichter[79,410], Markus Loeffler[571], Cristina López[262,558], Luisa Mantovani-Löffler[574], Peter Möller[575], German Ott[576], Bernhard Radlwimmer[410], Julia Richter[558,561], Marius Rohde[577], Philip C Rosenstiel[578], Andreas Rosenwald[579], Markus B Schilhabel[578], Matthias Schlesner[52,108], Stefan Schreiber[580], **Reiner Siebert#**[261,262], Peter F Stadler[276,277,280], Peter Staib[581], Stephan Stilgenbauer[582], Stephanie Sungalee[8], Monika Szczepanowski[561], Umut H Toprak[54,583], Lorenz HP Trümper[572], Rabea Wagener[262,558] and Thorsten Zenz[81]

Tumor Specific Providers – Germany (Pediatric Brain cancer)

Ivo Buchhalter[52,53,54], Juergen Eils[66,67], Roland Eils[52,54,66,67], Volker Hovestadt[410], Barbara Hutter[79,80,81], David TW Jones[300,301], Natalie Jäger[52], Christof von Kalle[83], Marcel Kool[97,300], Jan O Korbel[7,8], Andrey Korshunov[97], Pablo Landgraf[584], Chris Lawerenz[67], Hans Lehrach[585], **Peter Lichter#**[79,410], Paul A Northcott[586], Stefan M Pfister[97,300,587], Bernhard Radlwimmer[410], Guido Reifenberger[584], Matthias Schlesner[52,108], Hans-Jörg Warnatz[585], Joachim Weischenfeldt[8,111,112], Stephan Wolf[588], Marie-Laure Yaspo[585] and Marc Zapatka[410]

Tumor Specific Providers – Germany (Prostate cancer)

Yassen Assenov[589], Benedikt Brors[81,117,278], Juergen Eils[66,67], Roland Eils[52,54,66,67], Lars Feuerbach[117], Clarissa Gerhauser[284], Jan O Korbel[7,8], Chris Lawerenz[67], Hans Lehrach[585], Sarah Minner[590], Christoph Plass[284], **Guido Sauter#**[591], Thorsten Schlomm[112,592], Nikos Sidiropoulos[111], Ronald Simon[591], **Holger Sültmann#**[81,593], Hans-Jörg Warnatz[585], Dieter Weichenhan[284], Joachim Weischenfeldt[8,111,112] and Marie-Laure Yaspo[585]

Tumor Specific Providers – India (Oral cancer)

Nidhan K Biswas[594], Luca Landoni[426], Arindam Maitra[594], **Partha P Majumder#**[594] and **Rajiv Sarin#**[595]

Tumor Specific Providers – Italy (Pancreatic cancer)

Davide Antonello[426], Stefano Barbi[433], Claudio Bassi[426], Samantha Bersani[429], Giada Bonizzato[430], Cinzia Cantù[430], Ivana Cataldo[429,430], Sara Cingarlini[37], Vincenzo Corbo[430,433, 434], Angelo

P Dei Tos[596], Matteo Fassan[597], Sonia Grimaldi[430], Luca Landoni[426], Rita T Lawlor[430], Claudio Luchini[429], Andrea Mafficini[430], Giuseppe Malleo[426], Giovanni Marchegiani[426], Michele Milella[37], Marco Miotto[426], Salvatore Paiella[426], Antonio Pea[426], Paolo Pederzoli[426], Borislav C Rusev[430], Andrea Ruzzenente[426], Roberto Salvia[426], Maria Scardoni[429], **Aldo Scarpa#**[430], Elisabetta Sereni[426], Michele Simbolo[433], Nicola Sperandio[430], Giampaolo Tortora[37,38] and Caterina Vicentini[430]

Tumor Specific Providers – Japan (Biliary tract cancer)

Yasuhito Arai[33], Natsuko Hama[33], Nobuyoshi Hiraoka[598], Fumie Hosoda[33,599], Mamoru Kato[368], Hiromi Nakamura[33], Hidenori Ojima[600], Takuji Okusaka[601], **Tatsuhiro Shibata#**[33,34], Yasushi Totoki[33] and Tomoko Urushidate[34]

Tumor Specific Providers – Japan (Gastric cancer)

Hiroyuki Aburatani#[272], Yasuhito Arai[33], Masashi Fukayama[602], Natsuko Hama[33], Fumie Hosoda[33,599], Shumpei Ishikawa[603], Hitoshi Katai[604], Mamoru Kato[368], Hiroto Katoh[605], Daisuke Komura[603], Genta Nagae[272,283], Hiromi Nakamura[33], Hirofumi Rokutan[606], Mihoko Saito-Adachi[33], **Tatsuhiro Shibata#**[33,34], Akihiro Suzuki[272,607], Hirokazu Taniguchi[608], Kenji Tatsuno[272], Yasushi Totoki[33], Tetsuo Ushiku[602], Shinichi Yachida[33,609] and Shogo Yamamoto[272]

Tumor Specific Providers – Japan (Liver cancer)

Hiroyuki Aburatani[272], Hiroshi Aikata[610], Koji Arihiro[610], Shun-ichi Ariizumi[611], Keith A Boroevich[47,48], Kazuaki Chayama[610], Akihiro Fujimoto[48], Masashi Fujita[48], Mayuko Furuta[48], Kunihito Gotoh[612], Natsuko Hama[33], Takanori Hasegawa[86], Shinya Hayami[613], Shuto Hayashi[86], Satoshi Hirano[614], Seiya Imoto[85,86], Mamoru Kato[368], Yoshiiku Kawakami[610], Kazuhiro Maejima[48], Satoru Miyano[86], Genta Nagae[272,283], **Hidewaki Nakagawa#**[48], Hiromi Nakamura[33], Toru Nakamura[614], Kaoru Nakano[48], Hideki Ohdan[610], Aya Sasaki-Oku[48], **Tatsuhiro Shibata#**[33,34], Yuichi Shiraishi[86], Hiroko Tanaka[86], Yasushi Totoki[33], Tatsuhiko Tsunoda[47,219,220,221], Masaki Ueno[613], Rui Yamaguchi[86], Masakazu Yamamoto[611] and Hiroki Yamaue[613]

Tumor Specific Providers – Singapore (Biliary tract cancer)

Su Pin Choo[615], Ioana Cutcutache[267,318], Narong Khuntikeo[426,616], John R McPherson[267,318], Choon Kiat Ong[617], Chawalit Pairojkul[253], Irinel Popescu[618], **Steven G Rozen#**[267,268,318], **Patrick Tan#**[254,266,267,268] and **Bin Tean Teh#**[266,267,268,269,270]

Tumor Specific Providers – South Korea (Blood cancer)

Keun Soo Ahn[619], Hyung-Lae Kim[27], Youngil Koh[306,307] and **Sung-Soo Yoon#**[307]

Tumor Specific Providers – Spain (Chronic Lymphocytic Leukemia)

Marta Aymerich[620], **Elias Campo#**[621,622], Josep Ll Gelpi[46,70], Ivo G Gut[132,133], Marta Gut[132,133], Armando Lopez-Guillermo[623], Carlos López-Otín[624], Xose S Puente[625], Romina Royo[46] and David Torrents[46,109]

Tumor Specific Providers – United Kingdom (Bone cancer)

Fernanda Amary[626], Daniel Baumhoer[627], Sam Behjati[1], Bodil Bjerkehagen[628], **Peter J Campbell#**[1,2], **Adrienne M Flanagan#**[629], PA Futreal[522], Ola Myklebost[630], Nischalan Pillay[631], Patrick Tarpey[632], Roberto Tirabosco[633] and Olga Zaikova[634]

Tumor Specific Providers – United Kingdom (Chronic myeloid disorders)

Jacqueline Boultwood[635], David T Bowen[1], Adam P Butler[1], **Peter J Campbell#**[1,2], Mario Cazzola[636], Carlo Gambacorti-Passerini[186], Anthony R Green[294], Eva Hellstrom-Lindberg[637], Luca Malcovati[636], Sancha Martin[1,371], Jyoti Nangalia[638], Elli Papaemmanuil[1] and Paresh Vyas[310,639]

Tumor Specific Providers – United Kingdom (Esophageal cancer)

Yeng Ang[640], Hugh Barr[641], Duncan Beardsmore[642], Matthew Eldridge[293], **Rebecca C Fitzgerald#**[324], James Gossage[643], Nicola Grehan[324], George B Hanna[644], Stephen J Hayes[645,646], Ted R Hupp[647], David Khoo[648], Jesper Lagergren[637,649], Laurence E Lovat[251], Shona MacRae[397], Maria O'Donovan[324], J Robert O'Neill[650], Simon L Parsons[651], Shaun R Preston[652], Sonia Puig[653], Tom Roques[654], Grant Sanders[248], Sharmila Sothi[655], Simon Tavaré[293], Olga Tucker[656], Richard Turkington[657], Timothy J Underwood[658] and Ian Welch[659]

Tumor Specific Providers – United Kingdom (Prostate cancer)

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Tumor Specific Providers – United States (TCGA)

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