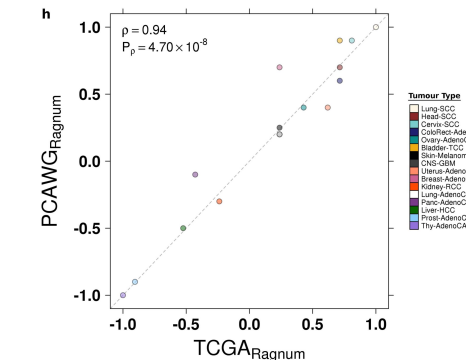
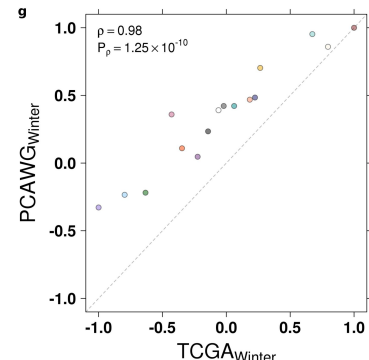
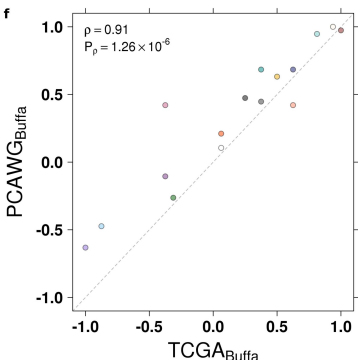
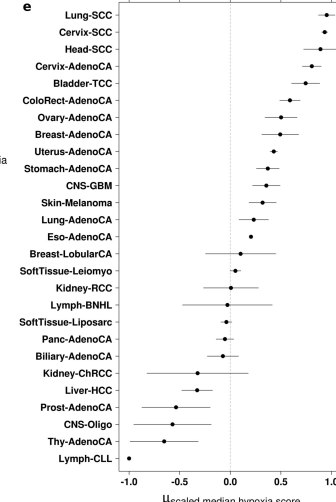
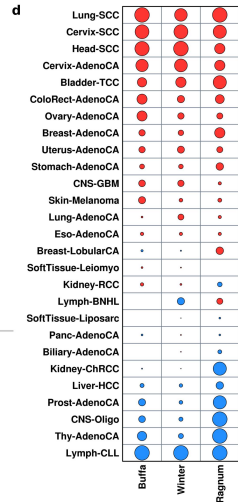
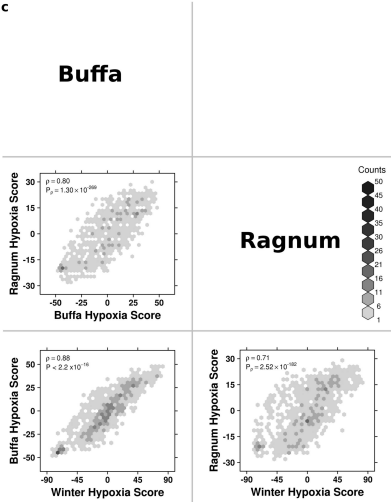
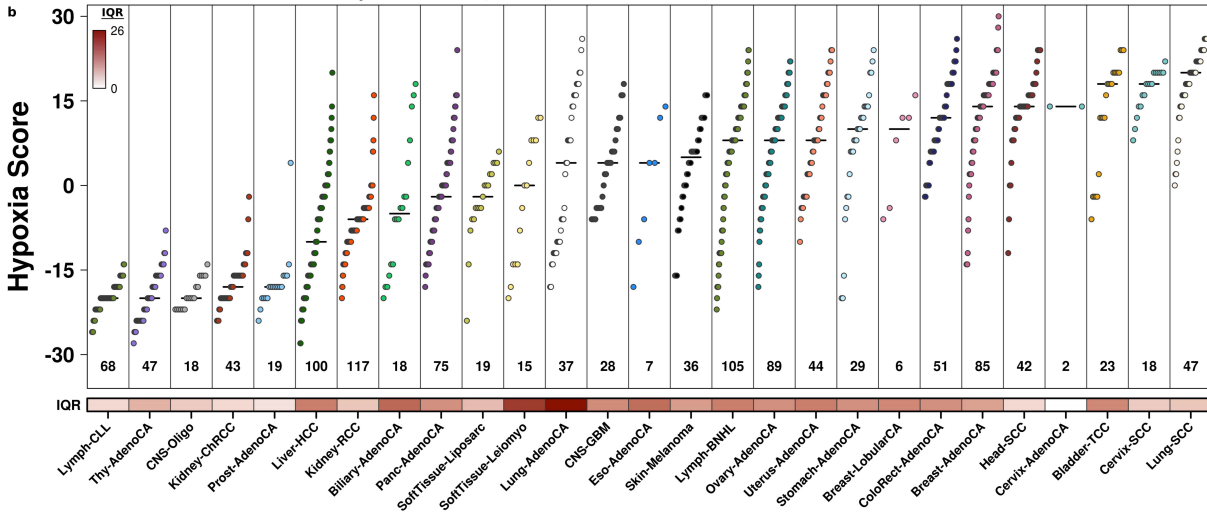
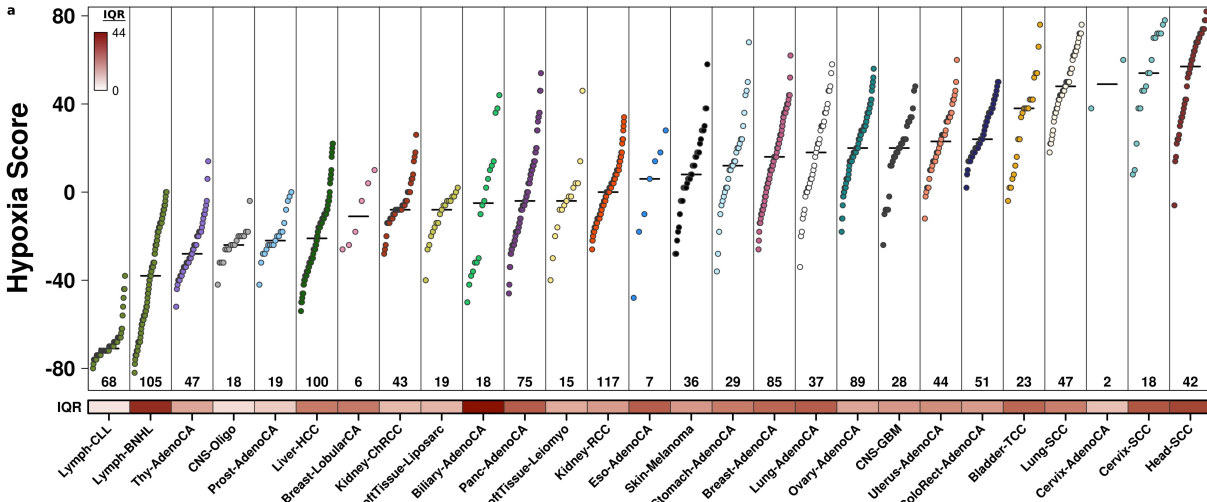


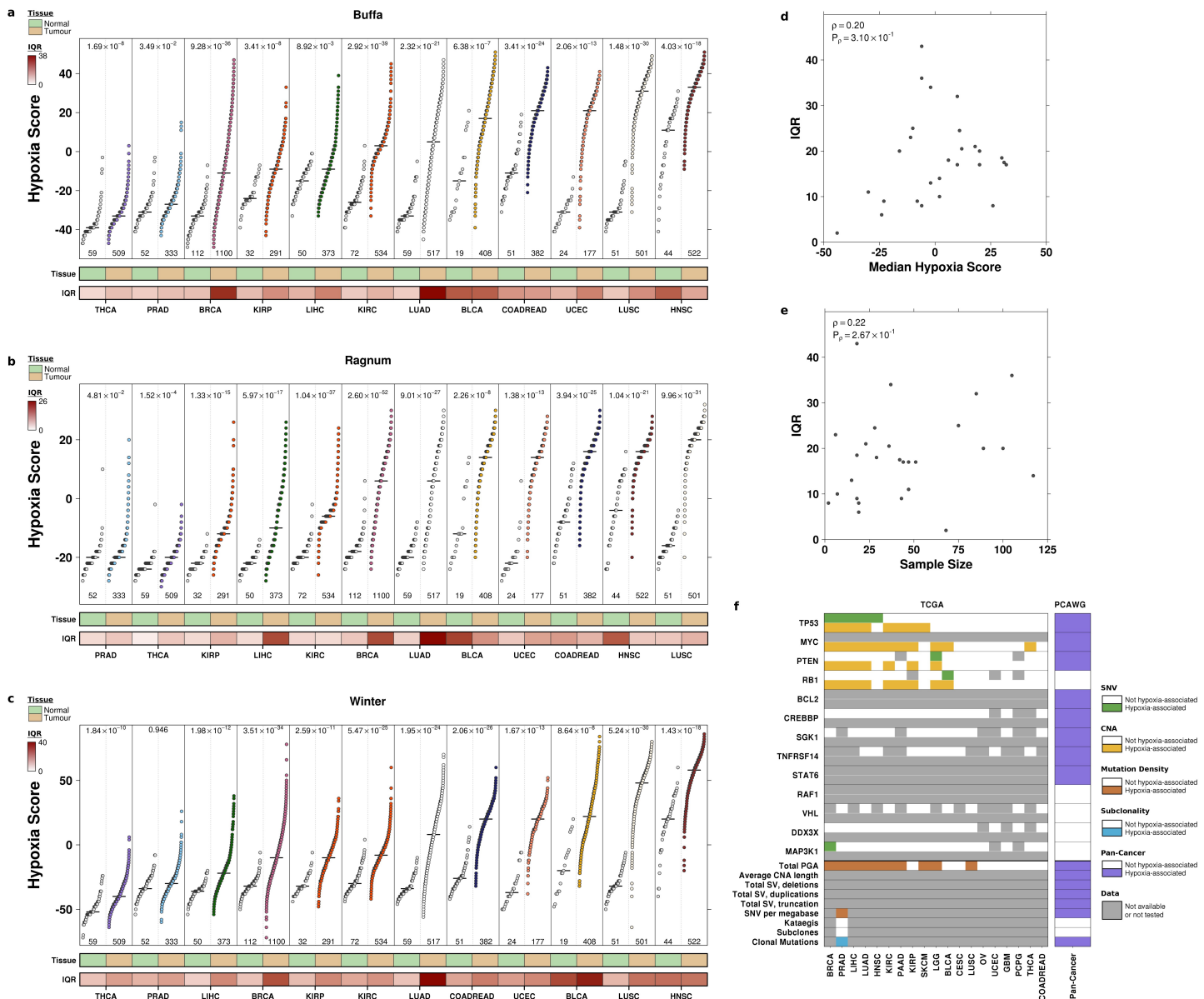
Supplementary Information for
“Divergent mutational processes distinguish hypoxic and normoxic tumours”

Bhandari *et al.*



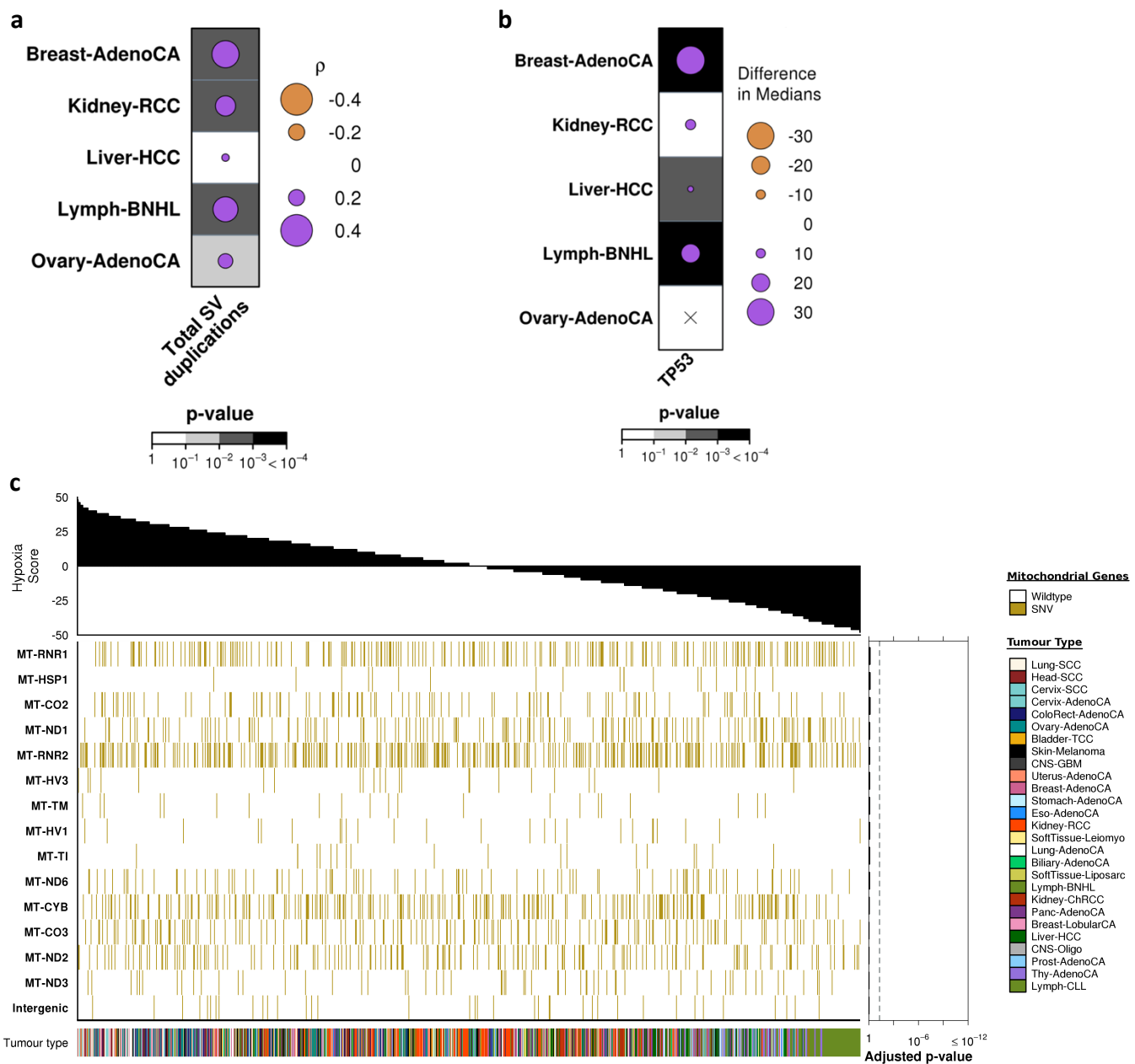
Supplementary Figure 1 – Pan-cancer landscape of hypoxia in primary tumours

Tumour hypoxia scores for 1,188 independent tumours from 27 cancer types based on the Winter¹ (a) and Ragnum² (b) hypoxia signatures. The black horizontal lines indicate the median hypoxia score within each cancer type. The number of tumours from each cancer type are shown along the bottom. IQR values for each cancer type are also shown along the bottom. c) Hypoxia scores based on the three independent signatures were highly correlated for 1,188 independent tumours from 27 cancer types. d) Comparison of median hypoxia scores within cancer types based on the Buffa³, Winter¹ and Ragnum² hypoxia signatures for 1,188 independent tumours from 27 cancer types. Median hypoxia values were scaled from +1 to -1. e) The mean of the scaled median hypoxia scores for each cancer type are shown by the filled circle. Lines show the standard deviation of the scaled median hypoxia score. Squamous tumours of the lung (Lung-SCC), cervix (Cervix-SCC) and head (Head-SCC) are amongst the most hypoxic cancer types. f-h) Association of hypoxia scores between 16 comparable types of cancer in PCAWG and TCGA. Dots represent the mean of the scaled median hypoxia scores from the Buffa³ (f), Winter¹ (g) and Ragnum² (h) hypoxia signatures. Pan-cancer calculations of hypoxia between the PCAWG (n = 1,188 independent tumours) and TCGA (n = 7,791 independent tumours) datasets is strongly correlated based on independent hypoxia signatures.



Supplementary Figure 2 – Hypoxia in tumour vs. normal samples and the genomics of hypoxia across cancers

Tumour samples consistently have elevated hypoxia compared to normal samples from the same tissue based on the Buffa (a), Ragnum (b) and Winter (c) hypoxia signatures ($n = 5,649$ independent tumours and $n = 625$ independent normal tissue samples). Bonferroni-adjusted p-values are shown along the top of each panel while sample sizes are shown along the bottom. The IQR values of cancer types were not associated with the median hypoxia score within that cancer type (d) or the sample size (e, $n = 1,188$ independent tumours). f) A partial summary of the knowledge around the genomics of hypoxic tumours. Hypoxia-related associations that have been previously examined within 19 tumour types in TCGA are shown along the left based on data from Bhandari *et al.*⁴ ($n = 7,791$ independent tumours). CNAs and SNVs in several genes were found to be associated with elevated hypoxia within tumour types. Hypoxia was also associated with elevated PGA in 10 tumour types. The right side of the figure partially summarizes the analyses carried out in this work ($n = 1,188$ independent tumours). Several of the previous intra-tumour type findings have been extended in this work as pan-cancer features of hypoxia and several novel features, particularly related to structural variants, have been assessed and found to be significantly associated with hypoxia. This is in addition to the novel pan-cancer work presented around single-base substitution signatures, indel signatures and tumour subclonality.



Supplementary Figure 3 – Confirmation of key hypoxia-associated features within individual tumour types and evaluation of hypoxia-associated mitochondrial mutations.

The number of duplications is significantly associated with tumour hypoxia within four of the five largest individual cancer types in our cohort (a). Dot sizes represent the Spearman's ρ and background shading represents p-values. For four of five histologies, the number of duplications were significantly positively correlated with hypoxia score, confirming the association previously described with a linear mixed-effects model across cancers. Tumours with *TP53* mutations are associated with elevated hypoxia within individual histologies (b). Dot sizes represent the difference in median hypoxia score between tumours that have a *TP53* mutation vs. tumours that have wildtype *TP53*. Background shading represents p-values (Mann-Whitney U-test). For all three histologies where *TP53* mutations are associated with hypoxia, the directionality of the association matches the directionality described in the pan-cancer analysis (*TP53* mutant tumours are associated with elevated hypoxia). For one histology, Ovary-AdenoCA, none of the tumours with information for mutational status and hypoxia were wildtype for *TP53*, so we could not evaluate if hypoxia scores were different between mutant and wildtype tumours. Results for a) and b) are shown for the five largest tumour types from the overall cohort of 1,188 tumours that have WGS and RNA-seq data. Mutations in the mitochondria were not associated with tumour hypoxia across cancer (c). Results are shown for the top 15 features based on FDR-adjusted p-values (n = 982 independent tumours).

Supplementary Table 1 – PCAWG cancer type codes

Cancer type codes for the 27 PCAWG cancer types examined in this study and their descriptions.

Cancer Type	Description
Biliary-AdenoCA	Biliary Adenocarcinoma
Bladder-TCC	Bladder Transitional Cell Carcinoma
Breast-AdenoCA	Breast Adenocarcinoma
Breast-LobularCA	Breast Lobular Carcinoma
CNS-GBM	CNS Glioblastoma
CNS-Oligo	CNS Oligodendroglioma
Cervix-AdenoCA	Cervix Adenocarcinoma
Cervix-SCC	Cervix Squamous Cell Carcinoma
ColoRect-AdenoCA	Colon/Rectum Adenocarcinoma
Eso-AdenoCA	Esophagus Adenocarcinoma
Head-SCC	Head/Neck Squamous Cell Carcinoma
Kidney-ChRCC	Kidney Chromophobe Renal Cell Carcinoma (Distal Tubules)
Kidney-RCC	Kidney Renal Cell Carcinoma (Proximal Tubules)
Liver-HCC	Liver Hepatocellular Carcinoma
Lung-AdenoCA	Lung Adenocarcinoma
Lung-SCC	Lung Squamous Cell Carcinoma
Lymph-BNHL	Lymphoid B-Cell Non-Hodgkin's Lymphoma
Lymph-CLL	Lymphoid Chronic Lymphocytic Leukemia
Ovary-AdenoCA	Ovary Adenocarcinoma
Panc-AdenoCA	Pancreas Adenocarcinoma
Prost-AdenoCA	Prostate Adenocarcinoma
Skin-Melanoma	Skin Melanoma
SoftTissue-Leiomyo	Leiomyosarcoma
SoftTissue-Liposarc	Liposarcoma
Stomach-AdenoCA	Stomach Adenocarcinoma
Thy-AdenoCA	Thyroid Adenocarcinoma
Uterus-AdenoCA	Uterus Adenocarcinoma

Supplementary Table 2 – Mutational density data by deciles

For each of the 15 mutational features analyzed, the value corresponding to each decile is provided. Decile are noted along the top row.

	0.00	0.10	0.20	0.30	0.40	0.50	0.60	0.70	0.80	0.90	1.00
Total SV, deletions	0.00	1.00	3.00	6.00	11.60	20.00	29.00	42.00	62.00	88.00	456.00
Total PGA, loss	0.00	0.60	5.13	6.09	9.20	14.19	19.95	26.27	31.81	39.64	60.53
Total PGA	0.00	5.01	8.68	14.21	20.54	27.99	36.79	45.15	54.33	64.93	92.41
Total SV, duplications	0.00	0.00	1.00	2.00	5.00	9.00	15.00	24.00	45.00	96.00	810.00
Average CNA length, loss	0.00	1.63E+06	4.08E+06	5.77E+06	7.70E+06	9.58E+06	1.21E+07	1.54E+07	2.17E+07	3.11E+07	8.78E+07
Total SV, truncation	0.00	0.00	1.00	3.00	5.00	8.00	14.00	22.00	39.20	67.10	1241.00
Average CNA length	0.00	1.86E+06	3.70E+06	5.19E+06	6.68E+06	8.48E+06	1.10E+07	1.47E+07	1.97E+07	2.92E+07	7.52E+07
Average CNA length, gain	0.00	0.00	8.14E+05	2.00E+06	3.15E+06	4.59E+06	6.42E+06	9.53E+06	1.52E+07	2.33E+07	9.73E+07
SNV per megabase	0.01	0.70	1.11	1.47	1.93	2.47	3.14	4.12	6.05	11.57	864.90
Total PGA, gain	0.00	0.00	0.84	3.84	6.12	8.78	12.33	17.68	24.32	35.68	89.89
Total SV, H-H Inversions	0.00	0.00	0.00	2.00	4.00	7.00	11.00	16.00	24.00	41.00	334.00
Total SV, T-T Inversions	0.00	0.00	1.00	2.00	4.00	7.00	11.00	16.00	24.00	39.00	327.00
Kataegis frequency	0.00	0.00	0.00	0.00	1.00	2.00	3.00	5.00	9.00	18.00	1.14E+04
CNA gain:loss	0.00	0.03	0.31	0.55	0.78	1.00	1.26	1.68	2.30	3.84	230.64
PGA gain:loss	0.00	0.00	0.15	0.29	0.43	0.62	0.85	1.10	1.76	4.25	1.24E+09

Supplementary Table 3 – Hypoxia associated mutational density features

Results from linear mixed-effect models associating hypoxia with mutational density features while controlling for cancer type, tumour purity, age and sex.

Mutational density feature	p-value	Bonferroni-adjusted p-value	R_{LMEM-C}^2	R_{LMEM-M}^2
total_sv_del	1.11E-10	1.66E-09	0.58924153	0.02343019
pga_loss	1.31E-08	1.97E-07	0.58527282	0.02136801
pga_total	2.41E-08	3.61E-07	0.57254909	0.02238394
total_sv_dup	0.00029372	0.00440584	0.59905876	0.00835183
avg_cna_loss_length	0.00198885	0.02983281	0.59654213	0.00670137
total_sv_tra	0.00329592	0.04943882	0.59688183	0.00615388
avg_cna_length	0.00351645	0.05274673	0.59262284	0.00645899
avg_cna_gain_length	0.0050237	0.07535548	0.6046345	0.00590894
MutsPerMb	0.00555344	0.08330165	0.60081588	0.00541866
pga_gain	0.02244465	0.3366697	0.59204366	0.00462285
total_sv_h2hinv	0.02431619	0.3647429	0.59589865	0.00460942
total_sv_t2tinv	0.03541738	0.53126077	0.59599525	0.00431923
frequency.kat	0.05983866	0.89757984	0.60187881	0.0039126
cna_gain_loss_ratio	0.13292578	1	0.60507099	0.00342699
pga_gain_loss_ratio	0.42345003	1	0.60311946	0.00274842

Supplementary Table 4– Hypoxia associated driver mutations

Results from linear mixed-effect models associating hypoxia with driver mutations while controlling for cancer type, tumour purity, age and sex.

Gene	p-value	FDR- adjusted p- value	R^2_{LMEM-C}	R^2_{LMEM-M}
<i>BCL2</i>	1.44E-17	7.56E-15	0.61524209	0.04529518
<i>TP53</i>	7.50E-15	1.97E-12	0.58702975	0.0426901
<i>MYC</i>	6.09E-07	0.00010659	0.59620501	0.01638566
<i>CREBBP</i>	7.15E-06	0.00093839	0.60491724	0.01269053
<i>SGK1</i>	6.36E-05	0.00667467	0.59914066	0.01064775
<i>TNFRSF14</i>	0.0001213	0.01061372	0.59489865	0.00979189
<i>PTEN</i>	0.00019948	0.01496111	0.59047392	0.00978797
<i>STAT6</i>	0.00044271	0.02905273	0.59430646	0.00833882
<i>VHL</i>	0.00068266	0.03982192	0.59985134	0.01449421
<i>RAF1</i>	0.00172618	0.09062425	0.59549027	0.0075624

Supplementary Table 5 – Hypoxia associated single base substitution signatures

Results from linear mixed-effect models associating hypoxia with the proportion of mutations attributed to single base substitution signatures while controlling for cancer type, tumour purity, age and sex.

Single-base substitution signature	p-value	FDR-adjusted p-value	R^2_{LMEM-C}	R^2_{LMEM-M}
SBS1	1.28E-09	8.33E-08	0.61063269	0.03315903
SBS5	4.41E-08	1.43E-06	0.58956286	0.02225793
SBS56	1.38E-05	0.00029993	0.61181946	0.01008063
SBS6	0.00013822	0.00197637	0.61060751	0.00858818
SBS3	0.00015203	0.00197637	0.60350628	0.01596484
SBS17b	0.00026168	0.0028349	0.60723431	0.0078508
SBS17a	0.00051701	0.0048008	0.606433	0.00723581
SBS21	0.00571373	0.0431149	0.60551536	0.00507594
SBS12	0.00596976	0.0431149	0.60361934	0.00664032

Supplementary Table 6 – Hypoxia associated small insertion and deletion signatures

Results from linear mixed-effect models associating hypoxia with the proportion of mutations attributed to small insertion and deletion signatures while controlling for cancer type, tumour purity, age and sex.

Insertion and deletion signature	p-value	FDR-adjusted p-value	R^2_{LMEM-C}	R^2_{LMEM-M}
ID6	3.39E-06	5.76E-05	0.60094444	0.01505225
ID5	0.00018121	0.00154028	0.59647682	0.01588363
ID9	0.00134169	0.00706468	0.60457952	0.00680836
ID2	0.00166228	0.00706468	0.60680165	0.01139191
ID8	0.00717277	0.02438742	0.60531094	0.0074097

Supplementary Table 7 – Associations of hypoxia with features of tumour clonality

Results from linear mixed-effect models associating hypoxia with features of tumour clonality while controlling for cancer type, tumour purity, age and sex. The features tested for associations with hypoxia include the total number of clonal alterations (clonal_total), the total number of clonal structural variants (clonal_SV), the total number of clonal indels (clonal_indel), the total number of clonal single nucleotide variants (clonal_SNV), the total number of subclonal alterations (subclonal_total) and the number of subclones detected in the tumour (subclone_number).

Clonality feature	p-value	Bonferroni-adjusted p-value	R^2_{LMEM-C}	R^2_{LMEM-M}
clonal_SV	1.96E-06	1.1746E-05	0.59553502	0.01329516
clonal_total	0.00077563	0.00465376	0.59915695	0.00741347
clonal_indel	0.00145617	0.00873701	0.60340965	0.00598623
clonal_SNV	0.00213627	0.01281765	0.59928141	0.00663105
subclone_number	0.0227242	0.13634518	0.60299828	0.00505359
subclonal_total	0.04626171	0.27757025	0.60214616	0.00392718

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4. Bhandari, V. *et al.* Molecular landmarks of tumor hypoxia across cancer types. *Nat. Genet.* **51**, 308–318 (2019).

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Novel somatic mutation calling methods

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Drivers and functional interpretation

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Integration of transcriptome and genome

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Integration of epigenome and genome

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

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Mutation signatures and processes

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Germline cancer genome

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Tumor subtypes and clinical translation

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Evolution and heterogeneity

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Exploratory: portals, visualization and software infrastructure

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Exploratory: mitochondrial variants and HLA/immunogenicity

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Exploratory: pathogens

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Tumor Specific Providers – Australia (Ovarian cancer)

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Tumor Specific Providers – Australia (Pancreatic cancer)

Matthew J Anderson¹⁸⁵, Davide Antonello⁴²⁴, Andrew P Barbour^{425,426}, Claudio Bassi⁴²⁴, Samantha Bersani⁴²⁷, **Andrew V Biankin**^{#359,360,361,362}, Timothy JC Bruxner¹⁸⁵, Ivana Cataldo^{427,428}, David K Chang^{360,362}, Lorraine A Chantrill³⁶⁰, Yoke-Eng Chiew⁴²¹, Angela

Chou^{360,429}, Angelika N Christ¹⁸⁵, Sara Cingarlini³⁷, Nicole Cloonan⁴³⁰, Vincenzo Corbo^{428,431,432}, Fraser R Duthie^{433,434}, J Lynn Fink^{105,185}, Anthony J Gill^{360,435}, Janet S Graham^{362,436}, **Sean M Grimmond**^{#363}, Ivon Harliwong¹⁸⁵, Oliver Holmes^{311,312}, Nigel B Jamieson^{361,362,437}, Amber L Johns^{360,420}, Karin S Kassahn^{185,417}, Stephen H Kazakoff^{311,312}, James G Kench^{360,435,438}, Luca Landoni⁴²⁴, Rita T Lawlor⁴²⁸, Conrad R Leonard^{311,312}, Andrea Mafficini⁴²⁸, Neil D Merrett^{424,439}, David K Miller^{185,360,420}, Marco Miotto⁴²⁴, Elizabeth A Musgrove³⁶², Adnan M Nagrial³⁶⁰, Felicity Newell^{311,312}, Katia Nones^{311,312}, Karin A Oien^{253,440}, Marina Pajic³⁶⁰, Ann-Marie Patch^{311,312}, John V Pearson^{311,312}, Mark Pinese³⁶⁰, Andreia V Pinho³⁶⁰, Michael C Quinn^{311,312}, Alan J Robertson¹⁸⁵, Ilse Rooman³⁶⁰, Borislav C Rusev⁴²⁸, Jaswinder S Samra^{424,435}, Maria Scardoni⁴²⁷, Christopher J Scarlett^{360,441}, Aldo Scarpa⁴²⁸, Elisabetta Sereni⁴²⁴, Katarzyna O Sikora⁴²⁸, Michele Simbolo⁴³¹, Morgan L Taschuk⁴⁵, Christopher W Toon³⁶⁰, Giampaolo Tortora^{37,38}, Caterina Vicentini⁴²⁸, Nick M Waddell³¹², Nicola Waddell^{311,312}, Scott Wood^{311,312}, Jianmin Wu³⁶⁰, Qinying Xu^{311,312} and Nikolajs Zeps⁴⁴²

Tumor Specific Providers – Australia (Skin cancer)

Lauri A Aaltonen⁴⁴³, Andreas Behren⁴⁴⁴, Hazel Burke⁴⁴⁵, Jonathan Cebon⁴⁴⁴, Rebecca A Dagg⁴⁴⁶, Ricardo De Paoli-Iseppi⁴⁴⁷, Ken Dutton-Regester³¹¹, Matthew A Field⁴⁴⁸, Anna Fitzgerald⁴⁴⁹, Sean M Grimmond³⁶³, **Nicholas K Hayward**^{#311,445}, Peter Hersey⁴⁴⁵, Oliver Holmes^{311,312}, Valerie Jakrot⁴⁴⁵, Peter A Johansson³¹¹, Hojabr Kakavand⁴⁴⁷, Stephen H Kazakoff^{311,312}, Richard F Kefford⁴⁵⁰, Loretta MS Lau⁴⁵¹, Conrad R Leonard^{311,312}, Georgina V Long⁴⁵², **Graham J Mann**^{#453,454}, Felicity Newell^{311,312}, Katia Nones^{311,312}, Ann-Marie Patch^{311,312}, John V Pearson^{311,312}, Hilda A Pickett⁴⁵¹, Antonia L Pritchard³¹¹, Gulietta M Pupo⁴⁵⁵, Robyn PM Saw⁴⁵², Sarah-Jane Schramm⁴⁵⁶, **Richard A Scolyer**^{#422,452,457,458}, Mark Shackleton^{188,218}, Catherine A Shang⁴⁵⁹, Ping Shang⁴⁵², Andrew J Spillane⁴⁵², Jonathan R Stretch⁴⁵², Varsha Tembe⁴⁵⁶, John F Thompson⁴⁵², Ricardo E Vilain⁴⁵⁷, Nick M Waddell³¹², Nicola Waddell^{311,312}, James S Wilmott⁴⁵², Scott Wood^{311,312}, Qinying Xu^{311,312} and Jean Y Yang⁴⁶⁰

Tumor Specific Providers – Canada (Pancreatic cancer)

John Bartlett^{461,462}, Prashant Bavi⁴⁶³, Ivan Borozan⁹, Dianne E Chadwick⁴⁶⁴, Michelle Chan-Seng-Yue⁴⁶³, Sean Cleary^{463,465}, Ashton A Connor^{466,467}, Karolina Czajka⁴⁶⁸, Robert E Denroche⁴⁶³, Neesha C Dhani⁴⁶⁹, Jenna Eagles⁷⁹, Vincent Ferretti^{45,69}, Steven Gallinger^{463,466,467}, Robert C Grant^{463,470}, David Hedley⁴⁶⁹, Michael A Hollingsworth⁴⁷¹, **Thomas J Hudson**^{#78,79}, Gun Ho Jang⁴⁶³, Jeremy Johns⁷⁹, Sangeetha Kalimuthu⁴⁶³, Sheng-Ben Liang⁴⁷², Ilinca Lungu^{463,473}, Xuemei Luo⁹, Faridah Mbabaali⁷⁹, **John D McPherson**^{#79,463,474}, Treasa A McPherson⁴⁷⁰, Jessica K Miller⁷⁹, Malcolm J Moore⁴⁶⁹, Faiyaz Notta^{463,475}, Danielle Pasternack⁷⁹, Gloria M Petersen⁴⁷⁶, Michael H A Roehr^{133,463,477,478,479}, Michelle Sam⁷⁹, Iris Selander⁴⁷⁰, Stefano Serra²⁵³, Sagedeh Shahabi⁴⁷², **Lincoln D Stein**^{#9,10}, Morgan L Taschuk⁴⁵, Sarah P Thayer¹⁰⁶, Lee E Timms⁷⁹, Gavin W Wilson^{9,463}, Julie M Wilson⁴⁶³ and Bradly G Wouters⁴⁸⁰

Tumor Specific Providers – Canada (Prostate cancer)

Timothy A Beck⁴⁵, Vinayak Bhandari⁹, Paul C Boutros^{9,133,142,143}, **Robert G
Bristow**^{#133,481,482,483,484}, Colin C Collins¹⁵¹, Shadrielle MG Espiritu⁹, Neil E Fleshner⁴⁸⁵, Natalie
S Fox⁹, Michael Fraser⁹, Syed Haider⁹, Lawrence E Heisler⁴⁸⁶, Vincent Huang⁹, Emilie Lalonde⁹,
Julie Livingstone⁹, John D McPherson^{79,463,474}, Alice Meng⁴⁸⁷, Veronica Y Sabelnykova⁹,
Adriana Salcedo⁹, Yu-Jia Shiah⁹, Theodorus Van der Kwast⁴⁸⁸ and Takafumi N Yamaguchi⁹

Tumor Specific Providers – China (Gastric cancer)

Shuai Ding⁴⁸⁹, Daiming Fan⁴⁹⁰, Yong Hou^{39,249}, Yi Huang^{153,154}, Lin Li³⁹, Siliang Li^{39,249},
Dongbing Liu^{39,249}, Xingmin Liu^{39,249}, **Youyong Lu**^{#28,29,30}, Yongzhan Nie^{490,491}, Hong Su^{39,249},
Jian Wang³⁹, Kui Wu^{39,249}, Xiao Xiao¹⁵⁴, Rui Xing^{29,492}, **Huanming Yang**^{#39}, Shanlin Yang⁴⁸⁹,
Yingyan Yu^{493, 230}, Xiuqing Zhang³⁹, Yong Zhou³⁹ and Shida Zhu^{39,249}

Tumor Specific Providers – EU: France (Renal cancer)

Rosamonde E Banks⁴⁹⁴, Guillaume Bourque^{495,496}, Alvis Brazma⁷, Paul Brennan⁴⁹⁷, **Mark
Lathrop**^{#496}, Louis Letourneau⁴⁹⁸, Yasser Riazalhosseini⁴⁹⁶, Ghislaine Scelo⁴⁹⁷, **Jörg Tost**^{#499},
Naveen Vasudev⁵⁰⁰ and Juris Viksna⁵⁰¹

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

Sung-Min Ahn⁵⁰², Ludmil B Alexandrov^{2,317}, Samuel Aparicio⁵⁰³, Laurent Arnould⁵⁰⁴, MR
Aure⁵⁰⁵, Shriram G Bhosle², E Birney⁷, Ake Borg⁵⁰⁶, S Boyault⁵⁰⁷, AB Brinkman⁵⁰⁸, JE Brock⁵⁰⁹,
A Broeks⁵¹⁰, Adam P Butler², AL Børresen-Dale⁵⁰⁵, C Caldas^{511,512}, Peter J Campbell^{1,2}, Suet-
Feung Chin^{511,512}, Helen Davies², C Desmedt⁵¹³, L Dirix⁵¹⁴, S Dronov², Anna Ehinger⁵¹⁵, JE
Eyfjord⁵¹⁶, GG Van den Eynden⁵¹⁷, A Fatima²¹⁷, Jorge Reis Filho⁵¹⁸, JA Foekens⁵¹⁹, PA
Futreal⁵²⁰, Øystein Garred^{521,522}, Moritz Gerstung^{7,8}, Dilip D Giri⁵¹⁸, D Glodzik², Dorthé
Grabau⁵²³, Holmfridur Hilmarsdottir⁵¹⁶, GK Hooijer⁵²⁴, Jocelyne Jacquemier⁵²⁵, SJ Jang⁵²⁶, Jon
G Jonasson⁵¹⁶, Jos Jonkers⁵²⁷, HY Kim⁵²⁵, Tari A King^{528,529}, Stian Knappskog², G Kong⁵²⁵, S
Krishnamurthy⁵³⁰, S Van Laere⁵¹⁴, SR Lakhani⁵³¹, A Langerød⁵⁰⁵, Denis Larsimont⁵³², HJ Lee⁵²⁶,
JY Lee⁵³³, Ming Ta Michael Lee⁵²⁰, Yilong Li², Ole Christian Lingjærde⁵³⁴, Gaetan
MacGrogan⁵³⁵, JW Martens⁵³⁶, Sancha Martin^{2,369}, Iñigo Martincorena², Andrew Menzies²,
Sandro Morganello², Ville Mustonen^{320,321,322}, Serena Nik-Zainal^{2,324,325,326}, Sarah O'Meara², I
Pauporté¹⁸, Sarah Pinder⁵³⁷, X Pivot⁵³⁸, Elena Provenzano⁵³⁹, CA Purdie⁵⁴⁰, Keiran M Raine², M
Ramakrishna², K Ramakrishnan², AL Richardson²¹⁷, M Ringnér⁵⁰⁶, Javier Bartolomé
Rodriguez¹⁰⁵, FG Rodríguez-González¹⁷⁵, G Romieu⁵⁴¹, Roberto Salgado²⁵³, Torill Sauer⁵³⁴, R
Shepherd², AM Sieuwerts¹⁷⁷, PT Simpson⁵³¹, M Smid⁵⁴², C Sotiriou⁵⁵, PN Span⁵⁴³, J Staaf⁵⁰⁶,
Lucy Stebbings², Ólafur Andri Stefánsson⁵⁴⁴, Alasdair Stenhouse⁵⁴⁵, **Michael Rudolf
Stratton**^{#2}, HG Stunnenberg^{249,546}, Fred Sweep⁵⁴⁷, BK Tan⁵⁴⁸, Jon W Teague², Gilles Thomas⁵⁴⁹,
AM Thompson⁵⁴⁵, S Tommasi⁵⁵⁰, I Treilleux^{551,552}, Andrew Tutt²¹⁷, NT Ueno³⁹³, Peter Van
Loo^{63,64}, P Vermeulen⁵¹⁴, Alain Viari⁴²⁸, MJ van de Vijver²⁵³, A Vincent-Salomon⁵⁴⁶, David C
Wedge^{2,354,355}, Bernice Huimin Wong⁵⁵³, Lucy Yates², X Zou², CHM van Deurzen⁵³⁶ and L van't
Veer^{554,555}

Tumor Specific Providers – Germany (Malignant lymphoma)

Ole Ammerpohl^{556,557}, Sietse Aukema^{558,559}, Anke K Bergmann⁵⁶⁰, Stephan H Bernhart^{276,277,281}, Hans Binder^{276,277}, Arndt Borkhardt⁵⁶¹, Christoph Borst⁵⁶², Benedikt Brors^{82,119,278}, Birgit Burkhardt⁵⁶³, Alexander Claviez⁵⁶⁴, Roland Eils^{52,54,66,67}, Maria Elisabeth Goebler⁵⁶⁵, Andrea Haake⁵⁵⁶, Siegfried Haas⁵⁶², Martin Hansmann⁵⁶⁶, Jessica I Hoell⁵⁶¹, Steve Hoffmann^{277,279,280,281}, Michael Hummel⁵⁶⁷, Daniel Hübschmann^{54,66,83,84,85}, Dennis Karsch⁵⁶⁸, Wolfram Klapper⁵⁵⁹, Kortine Kleinheinz^{52,54}, Michael Kneba⁵⁶⁸, Jan O Korbel^{7,8}, Helene Kretzmer^{277,281}, Markus Kreuz⁵⁶⁹, Dieter Kube⁵⁷⁰, Ralf Küppers⁵⁷¹, Chris Lawerenz⁶⁷, Dido Lenze⁵⁶⁷, Peter Lichter⁴⁰⁸, Markus Loeffler⁵⁶⁹, Cristina López^{262,556}, Luisa Mantovani-Löffler⁵⁷², Peter Möller⁵⁷³, German Ott⁵⁷⁴, Bernhard Radlwimmer⁴⁰⁸, Julia Richter^{556,559}, Marius Rohde⁵⁷⁵, Philip C Rosenstiel⁵⁷⁶, Andreas Rosenwald⁵⁷⁷, Markus B Schilhabel⁵⁷⁶, Matthias Schlesner^{52,110}, Stefan Schreiber⁵⁷⁸, **Reiner Siebert**^{#262,761}, Peter F Stadler^{276,277,281}, Peter Staib⁵⁷⁹, Stephan Stilgenbauer⁵⁸⁰, Stephanie Sungalee⁸, Monika Szczepanowski⁵⁵⁹, Umut H Toprak^{54,581}, Lorenz HP Trümper⁵⁷⁰, Rabea Wagener^{262,556} and Thorsten Zenz⁸²

Tumor Specific Providers – Germany (Pediatric Brain cancer)

Ivo Buchhalter^{52,53,54}, Juergen Eils^{66,67}, Roland Eils^{52,54,66,67}, Volker Hovestadt⁴⁰⁸, Barbara Hutter^{80,81,82}, David TW Jones^{301,302}, Natalie Jäger⁵², Christof von Kalle⁸⁴, Marcel Kool^{98,301}, Jan O Korbel^{7,8}, Andrey Korshunov⁹⁸, Pablo Landgraf⁵⁸², Chris Lawerenz⁶⁷, Hans Lehrach⁵⁸³, **Peter Lichter**^{#408}, Paul A Northcott⁵⁸⁴, Stefan M Pfister^{98,301,585}, Bernhard Radlwimmer⁴⁰⁸, Guido Reifenberger⁵⁸², Matthias Schlesner^{52,110}, Hans-Jörg Warnatz⁵⁸³, Joachim Weischenfeldt^{8,113,114}, Stephan Wolf⁵⁸⁶, Marie-Laure Yaspo⁵⁸³ and Marc Zapatka⁴⁰⁸

Tumor Specific Providers – Germany (Prostate cancer)

Yassen Assenov⁵⁸⁷, Benedikt Brors^{82,119,278}, Juergen Eils^{66,67}, Roland Eils^{52,54,66,67}, Lars Feuerbach¹¹⁹, Clarissa Gerhauser²⁸⁵, Jan O Korbel^{7,8}, Chris Lawerenz⁶⁷, Hans Lehrach⁵⁸³, Sarah Minner⁵⁸⁸, Christoph Plass²⁸⁵, **Guido Sauter**^{#589}, Thorsten Schlomm^{114,590}, Nikos Sidiropoulos¹¹³, Ronald Simon⁵⁸⁹, **Holger Sültmann**^{#82,591}, Hans-Jörg Warnatz⁵⁸³, Dieter Weichenhan²⁸⁵, Joachim Weischenfeldt^{8,113,114} and Marie-Laure Yaspo⁵⁸³

Tumor Specific Providers – India (Oral cancer)

Nidhan K Biswas⁵⁹², Luca Landoni⁴²⁴, Arindam Maitra⁵⁹², **Partha P Majumder**^{#592} and **Rajiv Sarin**^{#593}

Tumor Specific Providers – Italy (Pancreatic cancer)

Davide Antonello⁴²⁴, Stefano Barbi⁴³¹, Claudio Bassi⁴²⁴, Samantha Bersani⁴²⁷, Giada Bonizzato⁴²⁸, Cinzia Cantù⁴²⁸, Ivana Cataldo^{427,428}, Sara Cingarlini³⁷, Vincenzo Corbo^{428,431, 432}, Angelo P Dei Tos⁵⁹⁴, Matteo Fassan⁵⁹⁵, Sonia Grimaldi⁴²⁸, Luca Landoni⁴²⁴, Rita T Lawlor⁴²⁸, Claudio Luchini⁴²⁷, Andrea Mafficini⁴²⁸, Giuseppe Malleo⁴²⁴, Giovanni Marchegiani⁴²⁴, Michele Milella³⁷, Marco Miotto⁴²⁴, Salvatore Paiella⁴²⁴, Antonio Pea⁴²⁴, Paolo Pederzoli⁴²⁴, Borislav C Rusev⁴²⁸, Andrea Ruzzenente⁴²⁴, Roberto Salvia⁴²⁴, Maria Scardoni⁴²⁷, **Aldo Scarpa**^{#428}, Elisabetta Sereni⁴²⁴, Michele Simbolo⁴³¹, Nicola Sperandio⁴²⁸, Giampaolo Tortora^{37,38} and Caterina Vicentini⁴²⁸

Tumor Specific Providers – Japan (Biliary tract cancer)

Yasuhito Arai³³, Natsuko Hama³³, Nobuyoshi Hiraoka⁵⁹⁶, Fumie Hosoda^{33,597}, Mamoru Kato³⁶⁶, Hiromi Nakamura³³, Hidenori Ojima⁵⁹⁸, Takuji Okusaka⁵⁹⁹, **Tatsuhiko Shibata**^{#33,34}, Yasushi Totoki³³ and Tomoko Urushidate³⁴

Tumor Specific Providers – Japan (Gastric cancer)

Hiroyuki Aburatani^{#272}, Yasuhito Arai³³, Masashi Fukayama⁶⁰⁰, Natsuko Hama³³, Fumie Hosoda^{33,597}, Shumpei Ishikawa⁶⁰¹, Hitoshi Katai⁶⁰², Mamoru Kato³⁶⁶, Hiroto Katoh⁶⁰³, Daisuke Komura⁶⁰¹, Genta Nagae^{272,284}, Hiromi Nakamura³³, Hirofumi Rokutan⁶⁰⁴, Mihoko Saito-Adachi³³, **Tatsuhiko Shibata**^{#33,34}, Akihiro Suzuki^{272,605}, Hirokazu Taniguchi⁶⁰⁶, Kenji Tatsuno²⁷², Yasushi Totoki³³, Tetsuo Ushiku⁶⁰⁰, Shinichi Yachida^{33,607} and Shogo Yamamoto²⁷²

Tumor Specific Providers – Japan (Liver cancer)

Hiroyuki Aburatani²⁷², Hiroshi Aikata⁶⁰⁸, Koji Arihiro⁶⁰⁸, Shun-ichi Ariizumi⁶⁰⁹, Keith A Boroevich^{47,48}, Kazuaki Chayama⁶⁰⁸, Akihiro Fujimoto⁴⁸, Masashi Fujita⁴⁸, Mayuko Furuta⁴⁸, Kunihito Gotoh⁶¹⁰, Natsuko Hama³³, Takanori Hasegawa⁸⁷, Shinya Hayami⁶¹¹, Shuto Hayashi⁸⁷, Satoshi Hirano⁶¹², Seiya Imoto^{86,87}, Mamoru Kato³⁶⁶, Yoshiiku Kawakami⁶⁰⁸, Kazuhiro Maejima⁴⁸, Satoru Miyano⁸⁷, Genta Nagae^{272,284}, **Hidewaki Nakagawa**^{#48}, Hiromi Nakamura³³, Toru Nakamura⁶¹², Kaoru Nakano⁴⁸, Hideki Ohdan⁶⁰⁸, Aya Sasaki-Oku⁴⁸, **Tatsuhiko Shibata**^{#33,34}, Yuichi Shiraishi⁸⁷, Hiroko Tanaka⁸⁷, Yasushi Totoki³³, Tatsuhiko Tsunoda^{47,220,221,222}, Masaki Ueno⁶¹¹, Rui Yamaguchi⁸⁷, Masakazu Yamamoto⁶⁰⁹ and Hiroki Yamaue⁶¹¹

Tumor Specific Providers – Singapore (Biliary tract cancer)

Su Pin Choo⁶¹³, Ioana Cutcutache^{267,319}, Narong Khuntikeo^{424,614}, John R McPherson^{267,319}, Choon Kiat Ong⁶¹⁵, Chawalit Pairojkul²⁵³, Irinel Popescu⁶¹⁶, **Steven G Rozen**^{#267,268,319}, **Patrick Tan**^{#254,266,267,268} and **Bin Tean Teh**^{#266,267,268,269,270}

Tumor Specific Providers – South Korea (Blood cancer)

Keun Soo Ahn⁶¹⁷, Hyung-Lae Kim²⁷, Youngil Koh^{307,308} and Sung-Soo Yoon^{#308}

Tumor Specific Providers – Spain (Chronic Lymphocytic Leukemia)

Marta Aymerich⁶¹⁸, **Elias Campo**^{#619,620}, Josep Ll Gelpi^{46,71}, Ivo G Gut^{135,136}, Marta Gut^{135,136}, Armando Lopez-Guillermo⁶²¹, Carlos López-Otín⁶²², Xose S Puentes⁶²³, Romina Royo¹⁰⁵ and David Torrents^{105,111}

Tumor Specific Providers – United Kingdom (Bone cancer)

Fernanda Amary⁶²⁴, Daniel Baumhoer⁶²⁵, Sam Behjati², Bodil Bjerkehagen⁶²⁶, **Peter J Campbell**^{#1,2}, **Adrienne M Flanagan**^{#627}, PA Futreal⁵²⁰, Ola Myklebost⁶²⁸, Nischalan Pillay⁶²⁹, Patrick Tarpey⁶³⁰, Roberto Tirabosco⁶³¹ and Olga Zaikova⁶³²

Tumor Specific Providers – United Kingdom (Chronic myeloid disorders)

Jacqueline Boulton⁶³³, David T Bowen², Adam P Butler², **Peter J Campbell**^{#1,2}, Mario Cazzola⁶³⁴, Carlo Gambacorti-Passerini¹⁸⁶, Anthony R Green²⁹⁵, Eva Hellstrom-Lindberg⁶³⁵, Luca Malcovati⁶³⁴, Sancha Martin^{2,369}, Jyoti Nangalia⁶³⁶, Elli Papaemmanuil² and Paresch Vyas^{311,637}

Tumor Specific Providers – United Kingdom (Esophageal cancer)

Yeng Ang⁶³⁸, Hugh Barr⁶³⁹, Duncan Beardsmore⁶⁴⁰, Matthew Eldridge²⁹⁴, **Rebecca C Fitzgerald**^{#325}, James Gossage⁶⁴¹, Nicola Grehan³²⁵, George B Hanna⁶⁴², Stephen J Hayes^{643,644}, Ted R Hupp⁶⁴⁵, David Khoo⁶⁴⁶, Jesper Lagergren^{635,647}, Laurence E Lovat²⁵¹, Shona MacRae³⁹⁵, Maria O'Donovan³²⁵, J Robert O'Neill⁶⁴⁸, Simon L Parsons⁶⁴⁹, Shaun R Preston⁶⁵⁰, Sonia Puig⁶⁵¹, Tom Roques⁶⁵², Grant Sanders²⁴⁸, Sharmila Sothi⁶⁵³, Simon Tavaré²⁹⁴, Olga Tucker⁶⁵⁴, Richard Turkington⁶⁵⁵, Timothy J Underwood⁶⁵⁶ and Ian Welch⁶⁵⁷

Tumor Specific Providers – United Kingdom (Prostate cancer)

Nicholas Van As⁶⁵⁸, Daniel M Berney⁶⁵⁹, Johann S De Bono⁴⁰⁵, G Steven Bova³³⁰, Daniel S Brewer^{403,404}, Adam P Butler², Declan Cahill⁶⁵⁸, Niedzica Camacho⁴⁰⁵, **Colin S Cooper**^{#404,405,406}, Nening M Dennis⁶⁵⁸, Tim Dudderidge⁶⁵⁸, Sandra E Edwards⁴⁰⁵, **Rosalind A Eeles**^{#405,658}, Cyril Fisher⁶⁵⁸, Christopher S Foster^{660,661}, Mohammed Ghori², Pelvender Gill⁶³⁷, Vincent J Gnanapragasam^{383,662}, Gunes Gundem², Freddie C Hamdy⁶⁶³, Steve Hawkins²⁹⁴, Steven Hazell⁶⁵⁸, William Howat³⁸³, William B Isaacs²⁹², Katalin Karaszi⁶³⁷, Jonathan D Kay²⁵¹,

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Tumor Specific Providers – United States (TCGA)

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