Annex 6: Genomic alterations as putative predictive biomarkers for cancer therapy

Genes	Pathways	Aberration type	Disease examples	Putative or proven drugs
PIK3CA[51, 52], *PIK3R1* (Ref. 53), *PIK3R2*, *AKT1*, *AKT2* and *AKT3* (Refs 54,55)	Phosphoinositide 3-kinase (PI3K)	Mutation or amplification	Breast, colorectal and endometrial cancer	• PI3K inhibitors • AKT inhibitors
PTEN[56]	PI3K	Deletion	Numerous cancers	• PI3K inhibitors
MTOR[57], *TSC1*[58] and *TSC2* (Ref. 59)	mTOR	Mutation	Tuberous sclerosis and Bladder cancer	• mTOR inhibitors
RAS family (*HRAS*, *NRAS*, *KRAS*), *BRAF*[60] and *MEK1*	RAS–MEK	Mutation, rearrangement or amplification	Numerous cancers, including melanoma and prostate cancer	• RAF inhibitors • MEK inhibitors • PI3K inhibitors
Fibroblast growth factor receptor 1 (*FGFR1*), *FGFR2*, *FGFR3*, *FGFR4* (Ref. 36)	FGFR	Mutation, amplification or rearrangement	Myeloma, sarcoma and bladder, breast, ovarian, lung, endometrial and myeloid cancers	• FGFR inhibitors • FGFR antibodies
Epidermal growth factor receptor (*EGFR*)	EGFR	Mutation, deletion or amplification	Lung and gastrointestinal cancer	• EGFR inhibitors • EGFR antibodies
ERBB2 (Ref. 61)	ERBB2	Amplification or mutation	Breast, bladder, gastric and lung cancer	• ERBB2 inhibitors • ERBB2 antibodies
SMO[62, 63] and *PTCH1* (Ref. 64)	Hedgehog	Mutation	Basal cell carcinoma	• Hedgehog inhibitor
MET[65]	MET	Amplification or mutation	Bladder, gastric and renal cancer	• MET inhibitors • MET antibodies
JAK1, *JAK2*, *JAK3* (Ref. 66), *STAT1*, *STAT3*	JAK–STAT	Mutation or rearrangement	Leukaemia and lymphoma	• JAK–STAT inhibitors • STAT decoys
Discoidin domain-containing receptor 2 (*DDR2*)	RTK	Mutation	Lung cancer	• Some tyrosine kinase inhibitors

Erythropoietin receptor (*EPOR*)	JAK–STAT	Rearrangement	Leukaemia	• JAK–STAT inhibitors
Interleukin-7 receptor (*IL7R*)	JAK–STAT	Mutation	Leukaemia	• JAK–STAT inhibitors
Cyclin-dependent kinases (*CDKs*;[67] *CDK4*, *CDK6*, *CDK8*), *CDKN2A* and cyclin D1 (*CCND1*)	CDK	Amplification, mutation, deletion or rearrangement	Sarcoma, colorectal cancer, melanoma and lymphoma	• CDK inhibitors
ABL1	ABL	Rearrangement	Leukaemia	• ABL inhibitors
Retinoic acid receptor-α (*RARA*)	RARα	Rearrangement	Leukaemia	• All-trans retinoic acid
Aurora kinase A (*AURKA*)[68]	Aurora kinases	Amplification	Prostate cancer and breast cancer	• Aurora kinase inhibitors
Androgen receptor (*AR*)[69]	Androgen	Mutation, amplification or splice variant	Prostate cancer	• Androgen synthesis inhibitors • Androgen receptor inhibitors
FLT3 [70]	FLT3	Mutation or deletion	Leukaemia	• FLT3 inhibitors
MET	MET–HGF	Mutation or amplification	Lung cancer and gastric cancer	• MET inhibitors
Myeloproliferative leukaemia (*MPL*)	THPO, JAK–STAT	Mutation	Myeloproliferative neoplasms	• JAK–STAT inhibitors
***MDM2* (Ref. 71)**	MDM2	Amplification	Sarcoma and adrenal carcinoma	• MDM2 antagonist
KIT [72]	KIT	Mutation	GIST, mastocytosis, leukaemia	• KIT inhibitors
PDGFRA* and *PDGFRB	PDGFR	Deletion, rearrangement or amplification	Haematological cancer, GIST, sarcoma and brain cancer	• PDGFR inhibitors
Anaplastic lymphoma kinase (*ALK*)[9, 37, 73, 74]	ALK	Rearrangement or mutation	Lung cancer and neuroblastoma	• ALK inhibitors
RET	RET	Rearrangement or mutation	Lung cancer and thyroid cancer	• RET inhibitors
***ROS1* (Ref. 75)**	ROS1	Rearrangement	Lung cancer and cholangiocarcinoma	• ROS1 inhibitors
***NOTCH1* and**	Notch	Rearrangement	Leukaemia and	• Notch

NOTCH2	or mutation	breast cancer	signalling pathway inhibitors

CDKN2A, cyclin-dependent kinase inhibitor 2A; ERBB2, also known as HER2; GIST, gastrointestinal stromal tumour; FLT3, FMS-like tyrosine kinase 3; HGF, hepatocyte growth factor; JAK, Janus kinase; MEK, MAPK/ERK (mitogen-activated protein kinase/extracellular signal-regulated kinase) kinase; mTOR, mammalian target of rapamycin; PDGFR, platelet-derived growth factor receptor; PIK3R1, PI3K regulatory subunit 1; PIK3CA, PI3K catalytic subunit-α; PTCH1, Patched 1; PTEN, phosphatase and tensin homolog; RTK, receptor tyrosine kinase; SMO, Smoothened; STAT, signal transducer and activator of transcription; THPO, thrombopoietin; TSC1, tuberous sclerosis 1 protein.