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Review

Ion channel expression as promising cancer biomarker☆

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ABSTRACT

Cancer is a disease with marked heterogeneity in both response to therapy and survival. Clinical and histopathological characteristics have long determined prognosis and therapy. The introduction of molecular diagnostics has heralded an explosion in new prognostic factors. Overall, histopathology, immunohistochemistry and molecular biology techniques have described important new prognostic subgroups in the different cancer categories. Ion channels and transporters (ICT) are a new class of membrane proteins which are aberrantly expressed in several types of human cancers. Besides regulating different aspect of cancer cell behavior, ICT can now represent novel cancer biomarkers. A summary of the data obtained so far and relative to breast, prostate, lung, colorectal, esophagus, pancreatic and gastric cancers are reported. Special emphasis is given to those studies aimed at relating specific ICT or a peculiar ICT profile with current diagnostic methods. Overall, we are close to exploit ICTs for diagnostic, prognostic or predictive purposes in cancer. This article is part of a Special Issue entitled: Membrane channels and transporters in cancers.

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1. Introduction

Tumor diagnostics currently relies on imaging, laboratory tests (including tests for circulating tumor markers) and pathology on tumor samples, either biopsies or surgical specimens. Recent advancements in high-throughput genomics, proteomics and other -omics analyses, as well as high-content imaging modalities have greatly improved tumor diagnosis, with the aim of eventually optimizing treatment. We are now only a short distance away from using these prognostic factors

☆ This article is part of a Special Issue entitled: Membrane channels and transporters in cancers.

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Table 1
Ion channels and transporters discussed in the present review.

Channel type	Hgnc name	Iuphar name	Alternative names	Full name	Gene name	Chromosome location
Potassium	KCNA3	Kv1.3	MK3, HLK3, HPCN3	Potassium voltage-gated channel, Shaker-related subfamily, member 3	*KCNA3*	*1p13.3*
	KCNA5	Kv1.5	HK2, HPCN1	Potassium voltage-gated channel, Shaker-related subfamily, member 5	*KCNA5*	*12p13*
	KCNC1	Kv3.1	-	potassium voltage-gated channel, Shaw-related subfamily, member 1	*KCNC1*	*11p15*
	KCNC4	Kv3.4	-	Potassium voltage-gated channel, Shaw-related subfamily, member 4	*KCNC4*	*1p21*
	KCND1	Kv4.1	-	Potassium voltage-gated channel, Shal-related subfamily, member 1	*KCND1*	*Xp11.23*
	KCNE2	-	LQT6, MiRP1	Potassium voltage-gated channel, Isk-related subfamily, member 2	*KCNE2*	*21q22.1*
	KCNH1	K_v10.1	eag1	Potassium voltage-gated channel, subfamily H (eag-related), member 1	*hEAG1*	*1q32.2*
	KCNH2	K_v11.1	hERG1	Potassium voltage-gated channel, subfamily H (eag-related), member 2	*hERG1*	*7q36.1*
	KCNJ3	Kir3.1	GIRK1, KGA	Potassium inwardly-rectifying channel, subfamily J, member 3	*KCNJ3*	*2q24.1*
	KCNK2	K2p 2.1	TREK-1	Potassium channel, subfamily K, member 2	*KCNK2*	*1q41*
	KCNK9	K_{2P}9.1	TASK3	Potassium channel, subfamily K, member 5	*KCNK9*	*8q24.3*
	KCNK5	K_{2P}5.1	TASK2	Potassium channel, subfamily K, member 9	*KCNK5*	*6p21*
	KCNMA1	KCa1.1	mSLO1	Potassium large conductance calcium-activated channel, subfamily M, alpha member 1	*KCNMA1*	*10q22*
	KCNN4	KCa3.1	hSK4, hKCa4, hIKCa1	Potassium intermediate/small conductance calcium-activated channel, subfamily N, member 4	*KCNN4*	*19q13.2*
	KCNQ1	K_v7.1	KCNA9, KVLQT1	Potassium voltage-gated channel, KQT-like subfamily, member 1	*KCNQ1*	*11p15.5*
	KCNQ5	K_v7.5	-	Potassium voltage-gated channel, KQT-like subfamily, member 5	*KCNQ5*	*6q14*
Sodium	SCN5A	Na_v 1.5	-	Sodium channel, voltage-gated, type V, alpha subunit	*SCN5A*	*3p21*
	SCN9A	Na_v 1.7	-	Sodium channel, voltage-gated, type IX, alpha subunit	*SCN9A*	*2q24*
Calcium	ATP2B2	PMCA2	-	ATPase, Ca++ transporting, plasma membrane 2	*ATP2B2*	*3p25.3*
	ATP2C1	SPCA1	ATP2C1A, PMR1	ATPase, Ca++ transporting, type 2C, member 1	*ATP2C1*	*3q21.3*
	ATP2C2	SPCA2	KIAA0703	ATPase, Ca++ transporting, type 2C, member 2	*ATP2C2*	*16q24.1*
	CACNA1H	Cav3.2	-	Calcium channel, voltage-dependent, T type, alpha 1H subunit	*CACNA1H*	
	CACNA2D1	-	lncRNA-N3	Calcium channel, voltage-dependent, alpha 2/delta subunit 1	*CACNA2D1*	*7q21-q22*
	CACNA2D2	-	KIAA0558	Calcium channel, voltage-dependent, alpha 2/delta subunit 2	*CACNA2D2*	*3p21.3*
	CACNA2D3	-	HSA272268	Calcium channel, voltage-dependent, alpha 2/delta subunit 3	*CACNA2D3*	*3p21.1*
	CACNA2D4	-	-	calcium channel, voltage-dependent, alpha 2/delta subunit 4	*CACNA2D4*	*12p13.33*
	ORAI1	-	CRACM1, FLJ14466	ORAI calcium release-activated calcium modulator 1	*ORAI1*	*12q24.31*
	ORAI3	-	MGC13024	ORAI calcium release-activated calcium modulator 3	*ORAI3*	*16p11.2*
	TRPA1	TRPA1	ANKTM1	Transient receptor potential cation channel, subfamily A, member 1	*TRPA1*	*8q13*
	TRPC1	TRPC1	HTRP-1	Transient receptor potential cation channel, subfamily C, member 1	*TRPC1*	*3q23*
	TRPC3	TRPC3	-	Transient receptor potential cation channel, subfamily C, member 3	*TRPC3*	*4q27*
	TRPC4	TRPC4	HTRP4, TRP4	Transient receptor potential cation channel, subfamily C, member 4	*TRPC4*	*13q13.3*
	TRPC6	TRPC6	TRP6	Transient receptor potential cation channel, subfamily C, member 6	*TRPC6*	*11q22.1*
	TRPM7	TRPM7	CHAK1, TRP-PLIK, LTRPC7	Transient receptor potential cation channel, subfamily M, member 7	*TRPM7*	*15q21*
	TRPM8	TRPM8	-	Transient receptor potential cation channel, subfamily M, member 8	*TRPM8*	*2q37*
	TRPV1	TRPV1	-	Transient receptor potential cation channel, subfamily V, member 1	*TRPV1*	*17p13.2*
	TRPV4	TRPV4	OTRPC4, TRP12, VROAC, VRL-2, VR-OAC, CMT2C	Transient receptor potential cation channel, subfamily V, member 4	*TRPV4*	*12q24.1*
	TRPV6	TRPV6	CaT1	Transient receptor potential cation channel, subfamily V, member 6	*TRPV6*	*7q34*
Chloride	ANO1	CaCC	DOG1, FLJ10261, TAOS2	Anoctamin 1, calcium-activated chloride channel	*ANO1*	*11q13.2*
	CLCA1	-	CLCRG1	Chloride channel accessory 1	*CLCA1*	*1p22.3*
	CLCA2	-	CLCRG2	Chloride channel accessory 2	*CLCA2*	*1p22.3*
	CLCA4	-	CaCC2	Chloride channel accessory 4	*CLCA4*	*1p31-p22*
	CLIC1	-	NCC27, p64CLCP	Chloride intracellular channel 1	*CLIC1*	*6p21.3*
	CLIC3	-	-	Chloride intracellular channel 3	*CLIC3*	*9q34.3*
Aquaporins	AQP1	AQP1	CHIP28	Aquaporin 1 (Colton blood group)	*AQP1*	*7p14*
	AQP3	AQP3	GIL, “Gill blood group”	Aquaporin 3 (Gill blood group)	*AQP3*	*9p13*
	AQP5	AQP5	-	Aquaporin 5	*AQP5*	*12q13*
	AQP8	AQP8	-	Aquaporin 8	*AQP8*	*16p12*
	AQP9	AQP9	HsT17287, SSC1	Aquaporin 9	*AQP9*	*15q*
Anions	VDAC1	-	Outer Mitochondrial Membrane Protein Porin 1, PORIN	Voltage-Dependent Anion-Selective Channel Protein 1	VDAC1	*5q3.1*
Transporters	ABCA3	ABCA3	ABC-C, EST111653, LBM180	ATP-binding cassette, sub-family A (ABC1), member 3	*ABCA3*	*16p13.3*
	ABCB1	ABCB1	ABC20, CD243, GP170, “multidrug resistance protein 1”, P-gp	ATP-binding cassette, sub-family B (MDR/TAP), member 1	*ABCB1*	*7q21.12*
	ABCB4	ABCB4	GBD1, MDR2, PFIC-3	ATP-binding cassette, sub-family B (MDR/TAP), member 4	*ABCB4*	*7q21*
	ABCB11	ABCB11	ABC16, PFIC-2, PGY4, SPGP	ATP-binding cassette, sub-family B (MDR/TAP), member 11	*ABCB11*	*2q24*
	ABCC1	ABCC1	GS-X	ATP-binding cassette, sub-family C (CFTR/MRP), member 1	*ABCC1*	*16p13.1*
	ABCC3	ABCC3	cMOAT2, EST90757, MLP2, MOAT-D, MRP3	ATP-binding cassette, sub-family C (CFTR/MRP), member 3	*ABCC3*	*17q21*
	ABCC5	ABCC5	EST277145, MOAT-C, MRP5, SMRP	ATP-binding cassette, sub-family C (CFTR/MRP), member 5	*ABCC5*	*3q27*
	ABCC6	ABCC6	EST349056, MLP1, MRP6, URG7	ATP-binding cassette, sub-family C (CFTR/MRP), member 6	*ABCC6*	*16p13.11*
	ABCC7	CFTR	ABC35, CFTR/MRP, dJ760C5.1, MRP7, TNR-CFTR	Cystic fibrosis transmembrane conductance regulator (ATP-binding cassette sub-family C, member 7)	*ABCC7*	*7q31-q32*
	ABCC8	ABCC8	ABC36, HHF1, HI, MRP8, PHHI, SUR1, TNDM2	ATP-binding cassette, sub-family C (CFTR/MRP), member 8	*ABCC8*	*11p15.1*
	ABCC10	ABCC10	EST182763, MRP7, SIMRP7	ATP-binding cassette, sub-family C (CFTR/MRP), member 10	*ABCC10*	*6p12.3*
	ABCG2	ABCG2	ABCP, BCRP, CD338, EST157481, MXR	ATP-binding cassette, sub-family G (WHITE), member 2 (Junior blood group)	*ABCG2*	*4q22.1*