Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL

INIST-CNRS

Gene Section
Review

AQP1 (aquaporin 1 (Colton blood group))

Jean Loup Huret

jean-loup.huret@atlasgeneticsoncology.org

Published in Atlas Database: February 2019

Online updated version : http://AtlasGeneticsOncology.org/Genes/AQP1ID46249ch7p14.html
Printable original version : http://documents.irevues.inist.fr/bitstream/handle/2042/70645/02-2019-AQP1ID46249ch7p14.pdf
DOI: 10.4267/2042/70645

Abstract

Review on aquaporin-1 (AQP1), with data on DNA, on the protein encoded, and where the gene is implicated.

Keywords
Aquaporin-1; AQP1; Tissue water balance; Cell migration; Cell division; Cell adhesion; Cellular volume regulation; Apoptosis; Angiogenesis; Cell cycle; Cell proliferation; Cell membrane; Channel; Cell junction; WNT

Identity

Other names: CHIP28

HGNC (Hugo): AQP1

Location : 7p14.3

DNA/RNA

Transcription

There are various splicing forms.
Canonical form transcript (hg38), including UTRs: chr7:30,911,694 - 30,925,516, size: 13,823bp on forward (+) strand; coding region: chr7:30,911,910 - 30,923,629, size: 11,720bp, according to UCSC. Four exons: exon1 (nt 1 - 600) codes for amino acids (aa) 1-128, exon2 (nt 10373 - 10537) for aa 129-183; exon3 (nt 10871 - 10951) for aa 184-210, and exon4 (nt 11757 - 13823) for aa 211-269 (nextProt).

Protein

Aquaporins are a family of hydrophobic transmembrane channel proteins involved in transport of water and small molecules in response to osmotic gradients. They are distributed throughout many tissues, with various known roles of production, secretion, reabsorption and regulation of water, but also of cell migration (angiogenesis), signal transduction, and cell proliferation. There are 14 AQPs in humans (and 5 pseudogenes): MIP (previously called AQP0), AQP1, AQP2, AQP3, AQP4, AQP5, AQP6, AQP7, AQP8, AQP9, AQP10, AQP11, AQP12A and AQP12B. They are classified into two families: orthodox aquaporins, that transport water only, and aquaglyceroporins (AQP3, AQP7 and AQP9), which also transport glycerol, urea and other small molecules. AQPs form homo-tetramers (Review in Papadopoulos and Saadoun, 2015). The monomeric units of AQPs are ~30 kDa proteins and consist of 6 transmembrane α-helices (M1, M2, M4 to M6 and M8), 2 intramembrane half helices (M3 and M7), and 5 connecting loops (loops A to E) (Review in Verkman et al., 2014). They bear conserved intramembrane Asn-Pro-Ala (NPA) sequence motifs in the intramembrane domains, and six tilted transmembrane helices per monomer, with linkers (loops A to E). The NPA motifs act as hydrogen-bond donors and acceptors that coordinate the transport of water through the pore (Verkman et al., 2014).

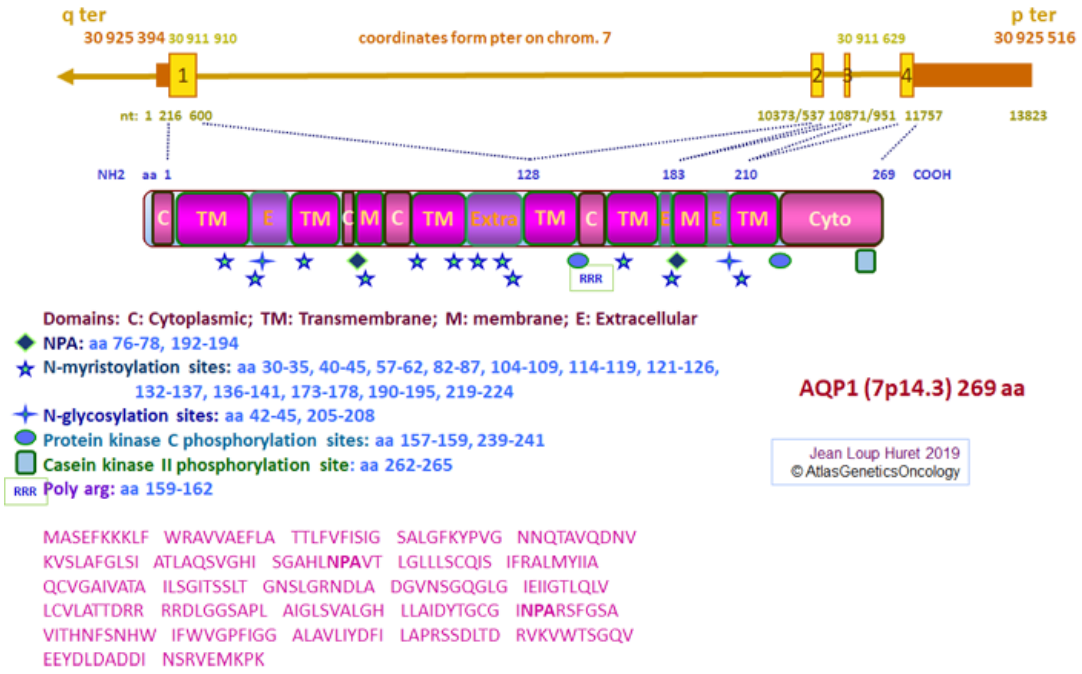

Figure 1. Aquaporin-1 (AQP1) gene exons and protein domains.

Description

Aquaporin-1 canonical form: 269 aa; 28.526kDa; other isoforms; 218, 186, and 154 aa. AQP1 is a transmembrane protein, with a N-term and a C-term cytoplasmic domains: amino acids 2 - 7 (Cytoplasmic), 8 - 36 (Transmembrane), 37 - 48 (Extracellular ("Loop A")), 49 - 66 (Transmembrane), 67 - 70 (Cytoplasmic), 71 - 84 (Intramembrane), 85 - 94 (Cytoplasmic ("Loop B"), 95 - 115 (Transmembrane), 116 - 136 (Extracellular ("Loop C")), 137 - 155 (Transmembrane), 156 – 166 (Cytoplasmic ("Loop D")), 167 - 183 (Transmembrane), 184 - 186 (Extracellular ("Loop E")), 187 - 200 (Intramembrane), 201 - 207 (Extracellular), 208 - 228 (Transmembrane), 229 - 269 (Cytoplasmic) (Figure. 1).

Helical subunits in Loop B and E juxtapose to form a water pore in the monomere.

The central pore of the homotetramer (Figure. 2) would be a path for ion and gas (Review in Tomita et al., 2017).

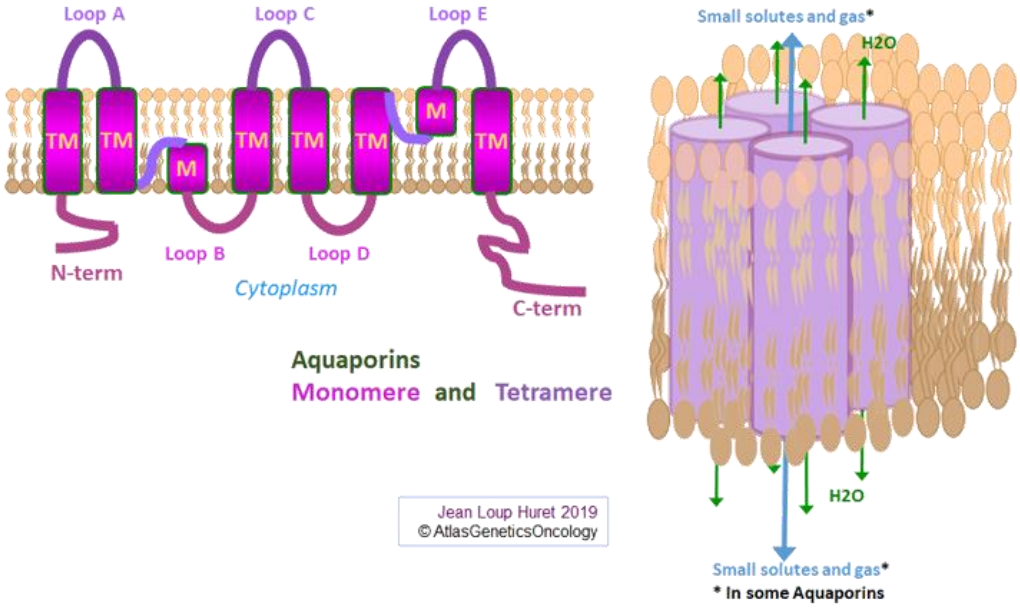

Figure 2. Aquaporins monomere and tetramere. Aquaporins are transmembrane proteins involved in transport of water and small molecules in response to osmotic gradients (water channels).

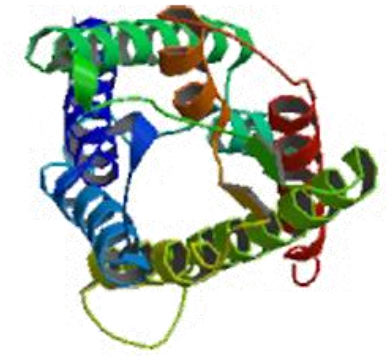

Figure 3. ModBase predicted comparative 3D structure.

Remarkable sites: (Figure. 1)
NPA: aa 76-78, 192-194
N-myristoylation sites (role in membrane targeting): aa 30-35, 40-45, 57-62, 82-87, 104-109, 114-119, 121-126, 132-137, 136-141, 173-178, 190-195, 219-224.
N-glycosylation sites: aa 42-45, 205-208.
Protein kinase C phosphorylation sites: aa 157 - 159, 239-241 (Thr 157 and 239); Casein kinase II phosphorylation site: aa 262 - 265 (Ser 262).
Poly Arg (for preventing proton conduction): aa 159-162.

Expression

AQPs are widely expressed. AQP1 is the main water channel in human (especially erythrocytes), but its function in water permeation can be alternatively supported by urea transporters SLC14A1 and SLC14A2 and glucose transporter SLC2A1 (GLUT1). The CO_2-transporting function of APQ1 is replaceable by RHAG gas channel. (Hsu 2018). AQP1 is expressed in all tissues, in particular in renal tubules, exocrine pancreas, neuropil (synaptically dense regions of brain), bile ducts, corneal endothelium, bone marrow, myoepithelial cells of breast and endothelial cells (The Human Protein Atlas). AQP1 is present in pleura and microvessels. AQP1 and AQP4 are expressed in the iris and ciliary epithelium and play important roles in regulating aqueous humor (review in Huber et al. 2012).
Choroid plexus epithelium: AQP1 is highly expressed in the apical side of choroid plexus epithelium, where it facilitates cerebrospinal fluid (CSF) secretion and intracranial pressure regulation (Longatti et al., 2006; review in Huber et al. 2012).
Renal proximal tubule and loop of Henle: mice deficient in AQP1 have a reduced ability to concentrate urine and there is also a moderate defective urinary concentrating ability in AQP1 deficient patients (King et al., 2001).

Erythrocyte: CO_2 metabolite enters erythrocytes via diffusion and/or gas channels (e.g. AQP1 and RHAG).
AQP1 is a H_2O/CO_2 channel in the erythrocyte. There are 160,000-200,000 copies of AQP1 on one erythrocyte membrane (Hsu 2018). AQP1 forms complex with SLC4A1 (band 3) and CA2 (carbonic anhydrase II) for intraerythrocytic CO_2/HCO_3 conversion in relation to desoxy-hemoglobin (Hsu 2018). 60% of CO_2 flux in or out of RBCs is via AQP1 gas channel. The rest of CO_2 flux is likely through another gas channel, RHAG, and/or direct diffusion (Hsu 2018).

Localisation

Localized to the plasma membrane.

Function

AQPs main's role is to maintain tissue water balance. AQPs also facilitate cell migration, cell proliferation and cell adhesion. Cell migration: AQPs concentrate at the leading end of migrating cells and facilitate the formation of the lamellipodium (Papadopoulos and Saadoun, 2015). Cell proliferation: AQPs may activates transduction pathways such as the mitogen-activated protein kinase pathways or the Wnt/ β-catenin signaling.
AQP1 may also be involved in down regulation of apoptosis. AQP1 up-regulation induces CTNNB1 (β-catenin) overexpression and serves as co-activator in the nucleus to activate Wnt responsive genes such as MYC, CCND1 (cyclin D1), JUN and FOSL1. AQP1 stabilises the cadherin/ CTNNB1/Lin7/F-actin complex to enhance the migratory and invasive capacity of tumor cells. AQP1 enhances the activity of MMP2 and MMP9 through PTK2 (FAK) and Wnt signalling pathways. Hypoxia induces AQP1 overexpression in tumour cells, in combination with important downstream effectors including CTNNB1, FAK and the Rho family of GTPases known for their role in tumorigenesis. (see review in Tomita et al., 2017).

Mutations

Germinal

Polymorphism: AQP1 is responsible for the Colton blood group system, with high incidence of Co(a) allele/antigen (Ala in aa 45), and low incidence of Co(b) allele/antigen (Val in aa 45). Colton-null phenotype Co(a-b-), is an aquaporin-1 deficiency. The patients, under stress, have a defect in urinary concentration capacity (King et al., 2002). AQP1-null mice have a significant decrease in urine osmolarity, but a normal survival.

Epigenetics

Increased expression of aquaporins 1 and 4 was found in Creutzfeldt-Jakob disease (Rodrèguez et al. 2006).

Implicated in

Aquaporin-1 is a well-established marker of proliferating tumor microvessels (Saadoun et al., 2002).
Aquaporin-1 is present in tumor vascular endothelium. AQP-expressing cancer cells show enhanced migration in vitro and greater local tumor invasion, tumor cell extravasation, and metastases in vivo than aquaporin-1-null transgenic mice. Aquaporin-1 facilitates endothelial cell migration and angiogenesis.

Astrocytoma

A t(1;7)(p13;p14) AQP1/ CHI3L2 has been found in low grade astrocytoma (Yoshihara et al., 2015).
The fusion gene ADCYAP1R1/AQP1 7p14-7p14 has been found in astrocytoma (Hu et al., 2018).
There was a significant increase in aquaporin-1 expression from low-grade to high-grade astrocytomas. AQP1 up-regulation was predominantly located perivascularly, and associated with angiogenesis, as well as with invasion of grade IV astrocytoma (El Hindy et al., 2013). Aquaporin-1 was expressed in microvessel endothelia and neoplastic astrocytes in metastatic carcinomas. Aquaporin-1 may participate in the formation of brain tumor edema (Saadoun et al., 2002).

Bladder urothelial carcinoma

Marked increase expression levels of aquaporin-1 was noted with bladder urothelial carcinoma histological grade and pathological stage. The expression of aquaporin-1 was markedly higher in cancerous tissues with lymph node metastasis (Liu et al., 2015).

Breast adenocarcinoma

A t(7;19)(p14;p13) AQP1/ TYK2 has been found in breast adenocarcinoma (Hu et al., 2018).
Aquaporin-1 is thought to be involved in estrogen mediated angiogenesis in the mammary gland (Mobasheri and Barrett-Jolley, 2014).

Cholangiocarcinoma

Strong aquaporin-1 expression predicts poor survival, regardless of pathological features in hilar cholangiocarcinoma (Li et al., 2017).

Choroid plexus carcinoma

Aquaporin-1 plays a role in tumor angiogenesis, cell migration, extravasation, and metastasis in choroid plexus carcinoma.

Colorectal cancer

Aquaporin-1 is an independent prognostic factor in advanced colon cancer (Yoshida et al., 2013). Expression of aquaporins 1, 3, and 5 was found in seven colon and colorectal cancer cell lines. The expression of aquaporins 1 and 5 was induced in early-stage disease (early dysplasia) and maintained through the late stages of colon cancer development (Moon et al., 2003).

Head and neck cancer

High expression is correlated with better prognosis in head and neck cancer, according to The Human Protein Atlas. On the other hand, aquaporin-1 was overexpressed in nasopharyngeal cancer tissues; migrated tumor tissue had even higher expression (Li and Zhang 2010).

Hemangioblastoma

Upregulation of aquaporin-1 expression was found in hemangioblastoma (Chen et al. 2006).

Kidney adenocarcinomay

A t(7;20)(p14;q13) AQP1/ ARFGEF2 has been found in adenocarcinoma of the kidney (Hu et al., 2018).
High expression is correlated with better prognosis in renal cell cancer according to The Human Protein Atlas.

Lung cancer

A t(6;7)(p21;p14) AQP1/ CFB has been found in lung adenocarcinoma (Hu et al., 2018).
Aquaporin-1 was overexpressed in adenocarcinoma and bronchoalveolar carcinoma, respectively, whereas all cases of squamous cell carcinoma and normal lung tissue were negative (Hoque et al., 2006).

Multiple myeloma

Patients with active multiple myeloma display significantly higher levels of aquaporin-1 than those with non-active multiple myeloma. Patients with monoclonal gammopathies of undetermined significance (MGUS) had lower levels of aquaporin-1 (Vacca et al. 2001).

Uterus cervical carcinoma

The fusion gene TRA2A/AQP1 (7p15-7p14) has been found in squamous cell carcinoma of the uterus cervix (Hu et al., 2018).
Aquaporins 1 and 3 were upregulated in cervical carcinoma, significantly increased in advanced stage disease, and patients with deeper tumor infiltration, lymph node metastases or larger tumor volume (Chen et al., 2014).

Uterus endometrial adenocarcinoma

A positive correlation between aquaporin-1,

microvascular density and vascular endothelial growth factor (VEGFA) expression in tumor progression of endometrial adenocarcinoma (Pan et al. 2008).

Pleural malignant mesothelioma

Expression of aquaporin-1 in malignant mesothelioma is an independent prognostic factor, irrespective of the type of treatment received. Expression of AQP1 by more than 50% of tumor cells was associated with prolonged survival (Kao et al., 2012).

Prostate adenocarcinoma

Aquaporin-1 overexpression was significantly associated with higher Gleason scores and is associated with prostate adenocarcinoma progression (Park and Yoon 2017).

To be noted

Aquaporin-targeted drugs: Heavy metal ions (mercury, silver, gold) are inhibitors of aquaporin-1. The Henle loop diuretic bumetanide and analogues AqB013 and AqF026 also inhibit aquaporin-1. The quaternary ammonium compound tetraethylammonium is an inhibitor of aquaporin-1 water permeability (Verkman et al., 2014; Tomita et al., 2017).

References

Chen R, Shi Y, Amiduo R, Tuokan T, Suzuk L. Expression and prognostic value of aquaporin 1, 3 in cervical carcinoma in women of Uygur ethnicity from Xinjiang, China. PLoS One. 2014;9(2):e98576

Chen Y, Tachibana O, Oda M, Xu R, Hamada J, Yamashita J, Hashimoto N, Takahashi JA. Increased expression of aquaporin 1 in human hemangioblastomas and its correlation with cyst formation. J Neurooncol. 2006 Dec;80(3):219-25

El Hindy N, Bankfalvi A, Herring A, Adamzik M, Lambertz N, Zhu Y, Siffert W, Sure U, Sandalcioglu IE. Correlation of aquaporin-1 water channel protein expression with tumor angiogenesis in human astrocytoma. Anticancer Res. 2013 Feb;33(2):609-13

Hoque MO, Soria JC, Woo J, Lee T, Lee J, Jang SJ, Upadhyay S, Trink B, Monitto C, Desmaze C, Mao L, Sidransky D, Moon C. Aquaporin 1 is overexpressed in lung cancer and stimulates NIH-3T3 cell proliferation and anchorage-independent growth. Am J Pathol. 2006 Apr;168(4):1345-53

Hsu K. Exploring the Potential Roles of Band 3 and Aquaporin-1 in Blood CO_2 Transport-Inspired by Comparative Studies of Glycophorin B-A-B Hybrid Protein GP.Mur. Front Physiol. 2018;9:733

Hu X, Wang Q, Tang M, Barthel F, Amin S, Yoshihara K, Lang FM, Martinez-Ledesma E, Lee SH, Zheng S, Verhaak RGW. TumorFusions: an integrative resource for cancer-associated transcript fusions. Nucleic Acids Res. 2018 Jan 4;46(D1):D1144-D1149

Huber VJ, Tsujita M, Nakada T. Aquaporins in drug discovery and pharmacotherapy. Mol Aspects Med. 2012 Oct-Dec;33(5-6):691-703

Kao SC, Armstrong N, Condon B, Griggs K, McCaughan B, Maltby S, Wilson A, Henderson DW, Klebe S. Aquaporin 1 is an independent prognostic factor in pleural malignant mesothelioma. Cancer. 2012 Jun 1;118(11):2952-61

King LS, Choi M, Fernandez PC, Cartron JP, Agre P. Defective urinary concentrating ability due to a complete deficiency of aquaporin-1 N Engl J Med 2001 Jul 19;345(3):175-9

King LS, Nielsen S, Agre P, Brown RH. Decreased pulmonary vascular permeability in aquaporin-1-null humans Proc Natl Acad Sci U S A 2002 Jan 22;99(2):1059-63

King TE Jr. Respiratory bronchiolitis-associated interstitial lung disease Clin Chest Med 1993 Dec;14(4):693-8

Li C, Li X, Wu L, Jiang Z. Elevated AQP1 Expression Is Associated With Unfavorable Oncologic Outcome in Patients With Hilar Cholangiocarcinoma Technol Cancer Res Treat 2017 Aug;16(4):421-427

Li Q, Zhang B. Expression of aquaporin-1 in nasopharyngeal cancer tissues J Otolaryngol Head Neck Surg 2010 Oct;39(5):511-5

Liu J, Zhang WY, Ding DG. Expression of aquaporin 1 in bladder uroepithelial cell carcinoma and its relevance to recurrence Asian Pac J Cancer Prev 2015;16(9):3973-6

Longatti P, Basaldella L, Orvieto E, Dei Tos A, Martinuzzi A. Aquaporin(s) expression in choroid plexus tumours Pediatr Neurosurg 2006;42(4):228-33

Meléndez, Fernádez y Cuxart, Muniesa. [Perspectives of promotion for current nurses] Caridad Cienc Arte 1970;7(22):7-8

Mobasheri A, Barrett-Jolley R. Aquaporin water channels in the mammary gland: from physiology to pathophysiology and neoplasia J Mammary Gland Biol Neoplasia 2014 Mar;19(1):91-102

Moon C, Soria JC, Jang SJ, Lee J, Obaidul Hoque M, Sibony M, Trink B, Chang YS, Sidransky D, Mao L. Involvement of aquaporins in colorectal carcinogenesis Oncogene 2003 Oct 2;22(43):6699-703

Papadopoulos MC, Saadoun S. Key roles of aquaporins in tumor biology Biochim Biophys Acta 2015 Oct;1848(10 Pt B):2576-83

Park JY, Yoon G. Overexpression of Aquaporin-1 is a Prognostic Factor for Biochemical Recurrence in Prostate Adenocarcinoma Pathol Oncol Res 2017 Jan;23(1):189-196

Rodríguez A, Pérez-Gracia E, Espinosa JC, Pumarola M, Torres JM, Ferrer I. Increased expression of water channel aquaporin 1 and aquaporin 4 in Creutzfeldt-Jakob disease and in bovine spongiform encephalopathy-infected bovine-PrP transgenic mice Acta Neuropathol 2006 Nov;112(5):573-85

Saadoun S, Papadopoulos MC, Davies DC, Bell BA, Krishna S. Increased aquaporin 1 water channel expression in human brain tumours Br J Cancer 2002 Sep 9;87(6):621-3

Tomita Y, Dorward H, Yool AJ, Smith E, Townsend AR,

Price TJ, Hardingham JE. Role of Aquaporin 1 Signalling in Cancer Development and Progression Int J Mol Sci 2017 Jan 29;18(2)

Vacca A, Frigeri A, Ribatti D, Nicchia GP, Nico B, Ria R, Svelto M, Dammacco F. Microvessel overexpression of aquaporin 1 parallels bone marrow angiogenesis in patients with active multiple myeloma Br J Haematol 2001 May;113(2):415-21

Verkman AS, Anderson MO, Papadopoulos MC. Aquaporins: important but elusive drug targets Nat Rev Drug Discov 2014 Apr;13(4):259-77

Yoshida T, Hojo S, Sekine S, Sawada S, Okumura T, Nagata T, Shimada Y, Tsukada K. Expression of aquaporin-1 is a poor prognostic factor for stage II and III colon cancer Mol Clin Oncol 2013 Nov;1(6):953-958

Yoshihara K, Wang Q, Torres-Garcia W, Zheng S, Vegesna R, Kim H, Verhaak RG. The landscape and therapeutic relevance of cancer-associated transcript fusions Oncogene 2015 Sep 10;34(37):4845-54

This article should be referenced as such:

Huret JL. AQP1 (aquaporin 1 (Colton blood group)). Atlas Genet Cytogenet Oncol Haematol. 2020; 24(1):22-27.