**Supplementary Table 1:** List of all the pathogenic variants and their associated protein changes in gene sequences

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Gene(s)** | **Protein change** | **Condition(s)** | **Clinical significance (Last reviewed)** | **Review status** | **GRCh38 Chromosome** | **GRCh38 Location** | **dbSNP ID** |
| IDUA|SLC26A1 | A75T | Mucopolysaccharidosis type 1|Hurler syndrome | Pathogenic(Last reviewed: Dec 3, 2019) | criteria provided, multiple submitters, no conflicts | 4 | 987873 | rs758452450 |
| CYP27B1 | R429P | not provided | Pathogenic(Last reviewed: Mar 14, 2016) | criteria provided, single submitter | 12 | 57763738 | rs568165874 |
| CYP27B1 | F443fs | not provided|Vitamin D-dependent rickets, type 1|Inborn genetic diseases | Pathogenic(Last reviewed: Jan 7, 2020) | criteria provided, multiple submitters, no conflicts | 12 | 57763698 - 57763699 | rs780950819 |
| HOGA1 | L268del, L105del | Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Nov 27, 2014) | no assertion criteria provided | 10 | 97601958 - 97601960 | rs796052092 |
| HOGA1 | M292T, M129T | Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Nov 27, 2014) | no assertion criteria provided | 10 | 97611550 | rs796052087 |
| HOGA1 | Q116\* | Primary hyperoxaluria, type III|not provided | Pathogenic(Last reviewed: May 9, 2019) | criteria provided, single submitter | 10 | 97599094 | rs767405535 |
| HOGA1 | A243D, A80D | Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Nov 27, 2014) | no assertion criteria provided | 10 | 97601884 | rs796052085 |
| HOGA1 | V245I, V82I | Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Nov 27, 2014) | no assertion criteria provided | 10 | 97601889 | rs755562733 |
| HOGA1 | R255\*, R92\* | Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Nov 27, 2014) | no assertion criteria provided | 10 | 97601919 | rs796052086 |
| HOGA1 | T280I, T117I | Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Nov 27, 2014) | no assertion criteria provided | 10 | 97611514 | rs756489804 |
| HOGA1 | R303C, R140C | Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Nov 27, 2014) | no assertion criteria provided | 10 | 97611582 | rs149150736 |
| HOGA1 | N103I | Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Nov 27, 2014) | no assertion criteria provided | 10 | 97598871 | rs796052089 |
| HOGA1 | L178P | Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Nov 27, 2014) | no assertion criteria provided | 10 | 97599744 | rs796052090 |
| HOGA1 | G325S, G162S | Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Nov 27, 2014) | no assertion criteria provided | 10 | 97611648 | rs777046879 |
| HOGA1 |  | Primary hyperoxaluria, type III|not provided | Pathogenic(Last reviewed: Dec 26, 2019) | criteria provided, multiple submitters, no conflicts | 10 | 97600168 | rs185803104 |
| HOGA1 |  | not provided|Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Dec 24, 2019) | criteria provided, single submitter | 10 | 97601990 | rs770050262 |
| HOGA1 | D53fs | Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Nov 27, 2014) | no assertion criteria provided | 10 | 97584861 | rs796052091 |
| HOGA1 | Y39\* | Primary hyperoxaluria, type III|not provided | Pathogenic(Last reviewed: Jan 16, 2019) | criteria provided, single submitter | 10 | 97584820 | rs746419489 |
| APRT | L110P | Adenine phosphoribosyltransferase deficiency | Pathogenic(Last reviewed: Sep 1, 2020) | no assertion criteria provided | 16 | 88810141 | rs104894508 |
| IDUA|SLC26A1 | Q70\* | Hurler syndrome|Mucopolysaccharidosis, MPS-I-H/S|Mucopolysaccharidosis, MPS-I-S|Mucopolysaccharidosis, MPS-I-S|not provided|Mucopolysaccharidosis, MPS-I-H/S|Hurler syndrome|Mucopolysaccharidosis type 1 | Pathogenic(Last reviewed: Dec 13, 2019) | criteria provided, multiple submitters, no conflicts | 4 | 987858 | rs121965020 |
| IDUA|SLC26A1 | Y64\* | Hurler syndrome | Pathogenic(Last reviewed: Aug 22, 2017) | criteria provided, single submitter | 4 | 987842 | rs121965022 |
| IDUA|SLC26A1 | R89Q | Mucopolysaccharidosis type 1|Hurler syndrome|Mucopolysaccharidosis, MPS-I-H/S | Pathogenic(Last reviewed: Mar 22, 2018) | criteria provided, single submitter | 4 | 987916 | rs121965029 |
| APRT | F174del | Adenine phosphoribosyltransferase deficiency | Pathogenic(Last reviewed: Sep 1, 2020) | criteria provided, single submitter | 16 | 88809718 - 88809720 | rs121912681 |
| APRT |  | Adenine phosphoribosyltransferase deficiency | Pathogenic(Last reviewed: Sep 1, 2020) | no assertion criteria provided | 16 | 88810420 - 88810421 | rs281860263 |
| APRT | M136T | APRT deficiency, Japanese type|Adenine phosphoribosyltransferase deficiency | Pathogenic(Last reviewed: Sep 1, 2020) | no assertion criteria provided | 16 | 88809834 | rs28999113 |
| APRT | D65V | Adenine phosphoribosyltransferase deficiency | Pathogenic(Last reviewed: Sep 1, 2020) | criteria provided, single submitter | 16 | 88810550 | rs104894506 |
| APRT | W98\* | Adenine phosphoribosyltransferase deficiency | Pathogenic(Last reviewed: Sep 1, 2020) | no assertion criteria provided | 16 | 88810450 | rs104894507 |
| APRT | K88fs | Adenine phosphoribosyltransferase deficiency | Pathogenic(Last reviewed: Sep 1, 2020) | no assertion criteria provided | 16 | 88810482 - 88810483 | rs281860265 |
| CYP27B1 | E189G | Vitamin D-dependent rickets type 1A | Pathogenic(Last reviewed: Mar 1, 2013) | no assertion criteria provided | 12 | 57765320 | rs118204012 |
| APRT |  | Adenine phosphoribosyltransferase deficiency | Pathogenic(Last reviewed: Sep 1, 2020) | no assertion criteria provided | 16 | 88809699 | rs387906584 |
| APRT | V150F | Adenine phosphoribosyltransferase deficiency | Pathogenic(Last reviewed: Sep 1, 2020) | no assertion criteria provided | 16 | 88809793 | rs281860266 |
| CYP27B1 | E211fs | Vitamin D-dependent rickets type 1A | Pathogenic(Last reviewed: Dec 1, 1997) | no assertion criteria provided | 12 | 57765170 | rs387906258 |
| HOGA1 | E315del, E152del | Primary hyperoxaluria, type III|not provided | Pathogenic(Last reviewed: Dec 23, 2019) | criteria provided, multiple submitters, no conflicts | 10 | 97611612 - 97611614 | rs397509360 |
| HOGA1 | G287V, G124V | not provided|Primary hyperoxaluria, type III | Pathogenic/Likely pathogenic(Last reviewed: Dec 16, 2018) | criteria provided, multiple submitters, no conflicts | 10 | 97611535 | rs138207257 |
| HOGA1 | R70P | Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Nov 27, 2014) | no assertion criteria provided | 10 | 97584912 | rs267606763 |
| HOGA1 | C257G, C94G | Primary hyperoxaluria, type III|not provided | Pathogenic/Likely pathogenic(Last reviewed: Nov 30, 2019) | criteria provided, multiple submitters, no conflicts | 10 | 97601925 | rs267606764 |
| CYP27B1 | G125E | Vitamin D-dependent rickets type 1A | Pathogenic(Last reviewed: Mar 5, 1998) | no assertion criteria provided | 12 | 57766019 | rs28934605 |
| CYP27B1 | R335P | Vitamin D-dependent rickets type 1A | Pathogenic(Last reviewed: Mar 5, 1998) | no assertion criteria provided | 12 | 57764510 | rs28934606 |
| CYP27B1 | P382S | Vitamin D-dependent rickets type 1A | Pathogenic(Last reviewed: Mar 5, 1998) | no assertion criteria provided | 12 | 57764169 | rs28934607 |
| CYP27B1 | T232fs | Vitamin D-dependent rickets type 1A | Pathogenic(Last reviewed: Dec 1, 1997) | no assertion criteria provided | 12 | 57765108 | rs387906259 |
| CYP27B1 | V88fs | not provided|Vitamin D-dependent rickets type 1A | Pathogenic(Last reviewed: Feb 13, 2018) | criteria provided, single submitter | 12 | 57766131 | rs387906260 |
| CYP27B1 | T321R | Vitamin D-dependent rickets type 1A | Pathogenic(Last reviewed: Nov 1, 1999) | no assertion criteria provided | 12 | 57764755 | rs118204007 |
| CYP27B1 |  | Vitamin D-dependent rickets type 1A | Pathogenic(Last reviewed: Nov 1, 1999) | no assertion criteria provided | 12 | 57765296 | rs761780097 |
| CYP27B1 | R389H | not provided|Vitamin D-dependent rickets, type 1|Vitamin D-dependent rickets type 1A | Pathogenic/Likely pathogenic(Last reviewed: Nov 7, 2018) | criteria provided, multiple submitters, no conflicts | 12 | 57764147 | rs118204009 |
| CYP27B1 |  | Vitamin D-dependent rickets type 1A | Pathogenic(Last reviewed: Jun 1, 2002) | no assertion criteria provided | 12 | 57766006 | rs770204470 |
| CYP27B1 | R389G | Vitamin D-dependent rickets type 1A | Pathogenic(Last reviewed: Jun 1, 2002) | no assertion criteria provided | 12 | 57764148 | rs118204010 |
| CYP27B1 | L343F | Vitamin D-dependent rickets type 1A | Pathogenic(Last reviewed: Mar 1, 2013) | no assertion criteria provided | 12 | 57764487 | rs118204011 |
| IDUA|SLC26A1 | Y64fs | Hurler syndrome|not provided|Mucopolysaccharidosis type 1 | Pathogenic/Likely pathogenic(Last reviewed: Jul 21, 2017) | criteria provided, multiple submitters, no conflicts | 4 | 987841 - 987842 | rs794727240 |
| APRT |  | Adenine phosphoribosyltransferase deficiency|not provided | Pathogenic(Last reviewed: Sep 16, 2019) | criteria provided, single submitter | 16 | 88810067 - 88810068 | rs745594160 |
| IDUA|SLC26A1 | G51D | Mucopolysaccharidosis type 1|Hurler syndrome|not provided | Pathogenic(Last reviewed: Jul 16, 2019) | criteria provided, multiple submitters, no conflicts | 4 | 987236 | rs794726877 |
| HOGA1 | P45L | Primary hyperoxaluria, type III | Pathogenic(Last reviewed: Nov 27, 2014) | no assertion criteria provided | 10 | 97584837 | rs764396564 |
| IDUA|SLC26A1 |  | Hurler syndrome|not provided|Mucopolysaccharidosis type 1 | Pathogenic/Likely pathogenic(Last reviewed: Oct 18, 2017) | criteria provided, multiple submitters, no conflicts | 4 | 987950 | rs398123259 |
| IDUA|SLC26A1 |  | Mucopolysaccharidosis type 1|not provided | Pathogenic(Last reviewed: Nov 22, 2019) | criteria provided, multiple submitters, no conflicts | 4 | 987119 - 987130 | rs398123260 |
| IDUA|SLC26A1 | P55fs | not provided | Pathogenic(Last reviewed: Mar 26, 2014) | criteria provided, single submitter | 4 | 987809 | rs727503966 |
| CYP27B1 | L58fs | not provided | Pathogenic(Last reviewed: Jan 19, 2018) | criteria provided, single submitter | 12 | 57766870 - 57766871 | rs763437121 |
| IDUA|SLC26A1 | M1T | Mucopolysaccharidosis type 1 | Pathogenic(Last reviewed: Oct 11, 2018) | criteria provided, single submitter | 4 | 987086 | rs753767675 |
| IDUA|SLC26A1 | R89W | Mucopolysaccharidosis type 1 | Pathogenic(Last reviewed: Aug 20, 2019) | criteria provided, multiple submitters, no conflicts | 4 | 987915 | rs754966840 |
| CYP27B1 | G102E | Vitamin D-dependent rickets, type 1|not provided | Pathogenic(Last reviewed: Jan 26, 2017) | criteria provided, single submitter | 12 | 57766088 | rs1057520815 |
|  |  | Vitamin D-dependent rickets, type 1 | Pathogenic(Last reviewed: Oct 9, 2016) | criteria provided, single submitter |  |  |  |
| HOGA1 |  | Primary hyperoxaluria, type III|not provided | Pathogenic/Likely pathogenic(Last reviewed: Dec 26, 2018) | criteria provided, multiple submitters, no conflicts | 10 | 97584826 | rs1419840309 |
| CYP27B1 | R453C | Vitamin D-dependent rickets, type 1 | Pathogenic(Last reviewed: May 28, 2019) | criteria provided, single submitter | 12 | 57763667 | rs767480544 |

**Supplementary Table 2:  (a)** Showing functional roles of urolithiasis genes and **(b)** associated proteins

|  |  |  |  |
| --- | --- | --- | --- |
| **S.No.** | **Genes** | **Functions** | **References** |
| **1.** | **VDR** | Modulates, citrate metabolism and transport of phosphate and calcium | (Cantonero et al., 2019a) |
| **2.** | **IL6, 1B** | Urinary chemokines, their level increases respective of infection in urolithiasis patients | (Culig et al., 2005) |
| **3.** | **SPP1** | Oesteopontin gene, its polymorphisms cause calcium oxalate urolithiasis | (Safarinejad et al., 2013) |
| **4.** | **PON1** | Protects against peroxidation | (Eroglu et al., 2013) |
| **5.** | **F2** | Urinary inhibition of stone formation and also found as matrix protein | (Safarinejad et al., 2013) |
| **6.** | **CASR** | Causes increased calcium excretion | (Taguchi et al., 2017) |
| **7.** | **ORA1** | Calcium channel subunit, a risk factor for kidney stones | (Taguchi et al., 2017) |
| **8.** | **KL** | Regulates phosphate and calcium homeostasis in kidneys | (Taguchi et al., 2017) |
| **9.** | **VKORC1** | Inhibitor of calcium oxalate stones | (Hu et al., 2014) |
| **10.** | **GGCX** | Located inside cytoplasm of renal tubular epithelial cells, its activity decreases in urolithilic patients | (Sughra et al., 2019) |
| **11.** | **CALCR** | A G-protein of both osteoclast and renal tubular cell, has shown to increase  susceptibility of urolithiasis in some polymorphism | (Qin et al., 2019) |
| **12.** | **HSPG2** | Causes calcium oxalate stone formation | (Onaran et al., 2009) |
| **13.** | **APRT** | Its deficiency leads to urolithiasis in children | (Kumar and AlAni, 2018) |
| **14.** | **ZNF365** | Known to code a isoform of vitamin D, talin; and also found associated with uric acid lithiasis | (Medina-Escobedo et al., 2014) |
| **15.** | **SLC26A1** | Anion exchanger, mutation causes hyperoxaluria | (Gee et al., 2016) |
| **16.** | **IL18** | Proinflammatory cytokine, causes calcium oxalate or calcium phosphate stones | (Lai et al., 2010) |
| **(b) Other associated proteins** | | | |
| **1.** | **HRH1** | Inhibits renal vasodilation and urethral contractions in renal colic | (Yilmaz et al., 2009) |
| **2.** | **FGA** | Stone matrix protein | (Benson et al., 1993) |
| **3.** | **ORAI 3** | Calcium sensor pore forming subunits, where their suppression causes urolithiasis | (Gombedza et al., 2019) |
| **4.** | **ORAI 2** | Calcium sensor pore forming subunits, where their suppression causes urolithiasis | (Taguchi et al., 2017) |
| **5.** | **PROZ** | Stone matrix protein | (Merchant et al., 2008) |
| **6.** | **HPRT1** | Causes hyperuricemia | (Mishima et al., 2020) |
| **7.** | **IL1A** | Causes pediatric nephrolithiasis | (Mittal et al., 2007) |
| **8.** | **APOA1** | Stone matrix protein | (Dussol et al., 1995a) |

**Supplementary Table 3:** List of urolithiasis genes and its function in prostate cancer

|  |  |  |  |
| --- | --- | --- | --- |
| **S.No** | **Gene** | **Function** | **Reference** |
| **1.** | **VDR** | Polygenic,  it has inverse relation with CaP | (BEYENE et al., 2020) |
| **2.** | **IL6** | Regulating immune responses, cell growth, differentiations and VEGF expressions | (Culig et al., 2005) |
| **3.** | **SPP1** | An extracellular matrix signature hub and plays role in metastasis | (Pang et al., 2019) |
| **4.** | **PON1** | Paraoxonase 1, anti oxidant | (Abd Al Hamid et al., 2020) |
| **5.** | **SOD2** | Helps in Neuroendocrine differentiation, also in metastasis and aggressiveness | (Miar et al., 2015) |
| **6.** | **IL1RN** | An anti-inflammatory cytokine | (Cheng et al., 2007) |
| **7.** | **IL18** | A proinflammatory cytokine, to escape immune surveillance in prostate cell lines | (Fujita et al., 2011) |
| **8.** | **CASR** | Transmembrane receptor, involved in calcium homeostasis or prostate cancer metastasis | (Ahearn et al., 2016), (Liao et al., 2006) |
| **9.** | **PLAU** | Level decreases | (Arcidiacono et al., 2014) |
| **10.** | **KL** | An anti-ageing gene, codes transmembrane proteins in renal tubes called Klotho | (Abolghasemi et al., 2019) |
| **11.** | **VKORC1** | Involved in enhancing the invasion and metastasis like angiogenesis and cell migration. | (Tew et al., 2017) |
| **12.** | **ORAI1** | Calcium channels, exploited by the cancer cancerous cells for  supporting its hallmarks like proliferation, apoptosis inhibition, migration and angiogenesis | (Cantonero et al., 2019b) |
| **13.** | **CP** | An antioxidant (glycoprotein) which binds to copper in oxidative stress | (Nayak et al., 2003) |
| **14.** | **GGCX** | Found as risk factor among several others | (Sughra et al., 2019) |

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