1. STUDIES INCLUDED

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|  | Author/Year  [Reference] | Type of Study | Population/  Sample | Findings | Additional Findings |
|  | Thomson, E,  2023 [42] | Case series | 13 | -CNV- 1.4Mb deletion at 17q12 in proband MRKHS. Contains the candidate genes *LHX1* and *HNF1B*.  - Other CNVs- duplication at 3q13. 12q13.13 in proband MRKHS contains three main genes—IFTP57, HHLA2 and MYH15  - Microdeletion at Xp22.33 within the upstream conserved non-coding elements enhancer region of SHOX gene  - duplication at 2q24.2 of proband MRKHS involved *PLA2R1*, *ITGB6* and *RBMS1* | SNP microarray analysis  Included the in-vivo study in mice |
|  | Ragitha, TS, 2023 [76] | Cohort | 32 with MA and/or gonadal dysgenesis | Single nucleotide variations in WNT4 gene (n=3). Synonymous polymorphism showed the absence of microRNA regulatory sites (n=1). A nucleotide substitution in intronic regions that did not affect the normal splicing mechanism (n=2) | Also included those with gonadal dysgenesis |
|  | Brakta, S, 2023 [98] | Case-control | 87 with MRKHS and available parents | 14 SVs were present in 17/87 (19.5%) of probands with MRKHS and included seven deletions, three duplications, one new translocation in 5/50 cells-t(7;14)(q32;q32), confirmation of a previously identified translocation-t(3;16)(p22.3;p13.3), and two aneuploidies | Optical genome mapping was performed to identify Structural variants (SVs) |
|  | Ma, C 2022  [59] | Cohort | 622 probands with MRKHS | 16 rare variants in TBX6 from the combined cohort, including 1 protein-truncating variant suggesting a causal role for 1. 7 were shown to induce a loss-of-function effect by impaired the normal splicing of TBX6 mRNA, decreased protein expression, perturbed transcriptional activity, and protein mislocalization. |  |
|  | Buchert, R,  2022 [53] | Case series | five MRKHS-discordant pairs of MZ twins  -1 had type-1  -4 had type-2  MRKHS | - mosaic variant in ACTR3B with a high allele frequency in the affected tissue, a low allele frequency in the blood of the affected twin and almost absent in the blood of the unaffected twin- ACTR3B- Pathogenic  -PAX8 variant- a variant of unknown significance  -missense variant in WNT9B- a variant of unknown significance  -detected a pathogenic variant in *GREB1L* in one twin pair and their unaffected mother (showing a reduced phenotypic penetrance)  -transcriptome- widespread perturbations largely similar to those in sporadic cases. -Transcriptional changes were enriched for terms associated with estrogen and its receptors | Genome sequencing of blood of both twins as well as transcriptome analysis of uterine tissue of the affected twin |
|  | Li, H 2022 [86] | Case control | 40 MRKHS and 140 individuals  controls | Four novel variations of EMX2 |  |
|  | Chu, C, 2022 [44] | Case series | 10 MRKHS individuals | Variants of nine genes: TBC1D1, KMT2D, HOXD3, DLG5, GLI3, HIRA, GATA3, LIFR, and CLIP1 (n = 9) |  |
|  | Dell’Edera D,2021 [137] | Case report | 1 | Microduplications in 22q11.21 |  |
|  | Chen N, 2021 [38] | Case control | 592 MRKHS individuals (442 Chinese and  150 of mixed ethnicity) 941 individual  controls | Variants of 7 genes: PAX8 (n = 4), BMP4 (n = 2), BMP7 (n = 2), TBX6 (n = 1), HOXA10 (n = 1), EMX2 (n = 1), and WNT9B (n = 1) | Included patients had unilateral renal aplasia/ectopic kidney, and cervicothoracic somite dysplasia association |
|  | Mikhael S, 2021 [39] | Cohort | 111 MRKHS individuals  type 1 (*n* = 82)  type-2 (*n* = 29) | Variants of: WNT4, LAMC1, RARA, HOXA10, PAX2, and WNT9B, TBX6, SHOX, MMP14, and LRP10 |  |
|  | Pontecorvi P,2021[45] | Cohort | 36 MRKHS individuals | Altered gene expression pattern in PRKX, MUC1, HOXC8, GREB1L |  |
|  | Hentrich T, 2020 [97] | Case control | 39 with MRKHS  type 1- 22  type 2- 17  30 patients with healthy endometrium | 1906 differentially expressed genes (DEGs) comprising 1236 up and  670 downregulated genes in MRKHS type 1 and 1174 DEGs with 801 up- and 373 downregulated genes in MRKHS type 2 were identified when compared to controls  -Gene expression changes during the menstrual cycle are missing in the endometrium of MRKHS patients | Also compared endometrial tissues. RNA-seq of endometrial tissue of uterus rudiments for transcriptome analysis |
|  | Jacquinet A,2020 [80] | Cohort | 9 families with CUAs and/or kidney  malformations  68 individuals with CUAs | Variants of GREB1L (n = 4 families and 5 individuals) | Also included family members with only kidney malformations |
|  | Anant M, 2020 [133] | Case report | 1 with MRKHS type 2 | 18p deletion (n = 1) |  |
|  | Smol T, 2020 [88] | Case report | 1 with MRKHS | Microdeletion in 2q12.1q14.1 (involving PAX8) and microdeletion of SHOX locus | Patient also had congenital hypothyroidism |
|  | Backhouse B, 2019 [43] | Cohort | 8 MRKHS patients  -6 had type-1  -2 had type-2 | -Microarray analysis identified a 0.6-Mb deletion in the 16p11.2 region in a patient with MRKHS type 2 (location 29,595,483–30,199,713), affected candidate gene TBX6  - Variants (n = 6) and a deletion (affecting TBX6) (n = 1) of 16p11.2 8 MRKHS and MURCS individuals  -16 rare nonsynonymous variants in MRKHS candidate genes across the cohort, including variants in several genes, such as LRP10 and DOCK4 | whole exome sequencing was used |
|  | Herlin M K, 2019 [79] | Case series | 4 (Three genera-tions family) | Variants of GREB1L |  |
|  | Pan H X, 2019 [41] | Case series | 9 MRKHS type 1 and their parents | De novo changes in BAZ2B, KLHL18, PIK3CD, SLC4A10 and TNK2 |  |
|  | Tewes A C, 2019 [58] | Case control | 26 MRKHS type 1  27 MRKHS type 2  135 individual controls | Variants and substitution of TBX6 (n = 4) | 72 individuals with  Müllerian duct fusion anomalies were also included |
|  | Takahashi K, 2018 [95] | Case control | 10 MRKHS, and 7 unaffected individuals | De novo variants of MYCBP2, NAV3, and PTPN3 (n = 3 families) and a variant of MYCBP2 (n = 1) | included three  MRKHS persons from trio-based families |
|  | Ledig S, 2018 [63] | Cohort | 103 individuals with CUAs | Microdeletions and microduplications in 17q12, 22q11.21, 9q33.1, 3q26.11 and 7q31.1. (n = 8) |  |
|  | AlSubaihin A, 2018 [74] | Case report | 1 | Tetrasomy of the pericentromeric region of chromosome 22 (n = 1) | The patient had CES with MRKHS |
|  | Eggermann T, 2018 [146] | Case series | MRKHS  Type 1- 53  Type 2-52 | MRKHS due to an ICR1 hypomethylation in 11p15.5. Failing to identify altered imprinting marks of differentially methylated regions PLAGL1, GRB10 and MEST, H19 and KCNQ1OT1, MEG3, SNRPN, DIRAS, NESPAS and GNAS. Abnormality present (n=1) absent (n=100) | Also included individuals with Silver Russel Syndrome |
|  | Eksi D, 2018  [57] | Cohort | 19 MRKHS individuals | Variants of BM8A, CMTM7, CCR4, TRIM71, CNOT10, TP63, EMX2, and CFTR (n = 4) |  |
|  | Zhang W, 2017 [68] | Case report | 1 MRKHS | Novel missense mutation in LHX1 (NM\_005568: c.G1108A, p.A370T) | Used whole-exome sequencing analysis |
|  | Williams L S, 2017 [66] | Cohort | 147 MRKHS from North America and Turkey | Copy number variants of WNT4, HNF1B, or LHX1 (n = 6), but no point change (n = 100) | Included MRKHS indivi-duals with family members affected, and singletons |
|  | Brucker SY  2017 [83] | Cohort | 93 MRKHS;  68 type 1  25 type 2 | Variants of OXTR (n = 18) and ESR1 (n = 1) |  |
|  | Xing Q, 2016 [81] | Case control | 200 individual controls | Missense change of DACT1 (n = 1) | Also included 100 individuals with other Müllerian duct  anomalies |
|  | Williams 2016 [40] | Case report | 1 individual with MRKHSS | A balanced chromosomal translocation involving chromosomes 3 and 16 |  |
|  | Waschk D E J, 2016 [54] | Case control | 109 MRKHS and  135 individual controls | Variant of WNT9B (n = 5) | Also included individuals with Müllerian duct  anomalies |
|  | McGowan R, 2015 [48] | Prospe ctive study | 11 with MRKHS | Microdeletion and microduplication 1q21.1, 7p14.3, 16p11.2, 17q12, and 22q11.21-q11.23 and possibly implicating several genes (LHX1, BBS9, HNF1b, and TBX6) (n = 9) | Included 24 individuals with other Müllerian disorders |
|  | Ma,W. 2015  [51] | Case control | 182 MRKHS; 155 type 1, 27 type 2 and 228 controls | Polymorphisms in WNT9B and PBX1; Epistatic effect of AMH, PBX1, WNT7A and WNT9B | All individuals were unrelated |
|  | Chen M J, 2015 [23] | Cohort | 7 MRKHS type 1 individuals | Deletions at 15q11.2 (80%), 19q13.31 (40%), 1p36.21 (40%) and 1q44 (40%) (n = 5),1q21.1 (n = 2). Damaging variants of HNRNPCL1, OR2T2, OR4M2, ZNF816 and PDE11A |  |
|  | Rall, K. 2015  [25] | Cohort | 5 MRKHS-discor -dant monozygotic twin pairs | Duplication of MMP14 and LRP10 (n = 1) affected twin |  |
|  | Liu S, 2015  [87] | Case control | 517 cases and 563 controls | Novel nonsense variants of EMX2 (n = 1) | Included individuals with incomplete Müllerian  Fusion |
|  | Tewes A C, 2015 [50] | Retrosp ective case control | 116 MRKHS and 94 individual control | Variants of RBM8A (n = 13) TBX6 (n = 5) | Also included 51 individuals with other MD abnormalities |
|  | Murry, 2015  [99] | Cohort | 20 individuals with CUA | No pathogenic Copy number changes (n = 20) |  |
|  | Wang M, 2014 [52] | Case control | 42 MRKHS and 42  individual controls | Variants of WNT9B (n = 1) |  |
|  | Herlin. 2014  [19] | Case report | 2 cousins with MRKHS | Familial occurrence of MRKHS and unilateral renal aplasia. Male cousins have unilateral renal aplasia. | Reported 67 familial cases of MRKHS with other associated anomalies |
|  | Nodale C, 2014 [46] | Case control | 16 MRKHS and 5 individual controls | Upregulation of MUC1 (n = 8) and significant upregulation of HOXC8 (n = 3). Downregulation of HOXB2 (n = 7) and HOXB5 (n = 7) and Notch ligands JAG1 (n = 6) and DLL1 (n = 5) |  |
|  | Ma, D. 2014 [22] | Case report | 1 with Müllerian  agenesis and hypothyroidism | Deletion at 2q13q14.2 (including PAX8) (n = 1) |  |
|  | Sandbacka M,2013  [56] | Case control | 112 MRKHS I and 200 individual control | Variations including 16p11.2 and 17q12 deletions (8/50) or variations in TBX6 or LHX1 in MA patients (30/112) | Controls were women with at least 1 child |
|  | Ekici AB, 2013 [119] | Case control | 20 MRKHS and 53 individual control | Variations HOXA10 and HOXA13 | Included 7 non-MRKHS  individuals with genital tract anomalies |
|  | Wang P, 2012 [100] | Case control | 15 with uterine aplasia and 192  ethnic-matched individual controls | Variant of PAX2 (n = 1) | Included 177 with  incomplete Müllerian fusion |
|  | Ledig S, 2012 [61] | Cohort | 23 MRKHS I  39 MRKHS II | No changes in HNF1B Variants of LHX1 (n = 1/62) | Included 2 patients with DM and learning disability |
|  | Xia M, 2012 [67] | Case control | 96 with  CUAs and 105 individual controls | No significant variants (n = 0/96) but a rare polymorphism of LHX1 (n = 1/77) | Looked for variants of LHX |
|  | Hinkes B, 2012 [62] | Case report | 1 with MRKHS | Microdeletion in 17q12 (involving HNF1b and LHX1) (n = 1) | The patient also had unilateral renal aplasia |
|  | Chang X, 2012 [101] | Case series | 10 MRKHS | No perturbation that indicates the significance of WNT4 | Included 5 subjects with Müllerian aplasia and 174 incomplete Müllerian fusion |
|  | Ravel C, 2012 [82] | Case control | 12 MRKHS individuals | No significant changes were observed between the MRKHS individuals and the control group for LAMC1 and DLGH1 gene polymorphisms. |  |
|  | Philibert P  2011[75] | Cohort | 4 MRKHS | Wnt4 mutation | Included those with Mullerian duct abn. and hyperandrogenism |
|  | Ledig S, 2011 [21] | Cohort | 56 MRKHS individuals | Microdeletions and -duplications in 1q21.1, 17q12, and 22q11.21 involving LHX1 and HNF1B gene (n = 48) |  |
|  | Ma J, 2011 [90] | Cohort | 192 Chinese individuals with CUAs | Polymorphisms in PBX1 (n = 2) |  |
|  | Sandbacka M, 2011 [146] | Cohort | 83 individuals with CUAs | No association between hypomethylation of the H19 imprinted control region but aberrant methylation (n = 3/16) |  |
|  | Nik-Zainal S, 2011[55] | Cohort | 38 MRKHS I  25 MRKHS II | Microdeletion at 16p11.2 (n = 4), microdeletion at 17q12 (n = 4), 22q11.2 (n = 1) | Included isolated and syndromic MA |
|  | Rall K, 2011  [32] | Case control | 8 MRKHS and 8 individual controls | 293 genes with altered expression and 194 genes differentially methylated. |  |
|  | Morcel K, 2011 [72] | Cohort | 57 MRKHS individuals | Deletion in 4q34-qter, 8p23.1, 10p14 and 22q11.2 (n = 4) | Included individuals with DiGeorge syndrome and other multiple abnormalities |
|  | Gervasini C, 2010 [89] | Case control | 30 MRKHS and 53 individual controls | Partial duplication of SHOX (n = 5) |  |
|  | Acién P, 2010 [105] | Case report | 1 MRKHS | No microdeletions in 17q12 and 22q11.21 (n = 1) | The patient also had  pulmonary hypoplasia |
|  | Oram RA, 2010 [69] | Cohort | 58 individuals with isolated CUAs | Variants or deletion of HNF1B (n = 9/50 individuals with both CUAs and renal abnormalities) | Included 50 individuals with both CUAs and renal abnormalities |
|  | Liatsikos S A, 2010 [102] | Case control | 30 with MDAs and  100 individual controls | No causative variants of HOX A10 and HOX A11 |  |
|  | Ravel C, 2009 [122] | Cohort | 11 MRKHS individuals | Variants of WNT4, WNT5A, WNT7A, and WNT9B |  |
|  | Bernardini L,2009 [60] | Case series | 22 MRKHS individuals | Deletion in 17q12 (involving TCF2 and LHX1 genes) (n = 2) |  |
|  | Hofstetter G,2008 [103] | Case report | 1 MURCS | No major deletions or duplications in 22q11.1 12q24.1. and 3q27 (n = 1) |  |
|  | Lalwani S, 2008 [94] | Case control | 26 individuals with CUAs 30 controls | No HOXA10 gene variants |  |
|  | Philibert P, 2008 [121] | Case control | 28 individuals with CUAs and 100 controls | Variants of WNT4 gene |  |
|  | Mencarelli M A, 2008  [64] | Case series | 84 with mental problems and  Uterine aplasia | Deletions in 7q31, 14q21.1, Xq25 and duplications in 12p11.22, 12q21.31, 13q31.1, 17q12, Xp22.31, Xq28 (n=10 CNVs). Parents were healthy | Primarily included individuals with mental problems |
|  | Miyamoto 2008 [85] |  | Human and other animal models | Showed GATA4 a key regulator of gonadal development by regulating SRY and AMH |  |
|  | Drummond JB, 2008 [93] | Cohort | 12 MRKHS patients | No variants of the GSK-3beta phosphorylation sites on exon 3 of  beta-catenin gene (n = 12) |  |
|  | Sundaram U T, 2007 [71] | Case report | 2 with absent uterus | Deletion in 22q11.2 (n = 2) | Both patients had MA and unilateral renal agenesis |
|  | Biason-Lauber A, 2007 [120] | Case report | 1 with MRKHS | Variants of WNT4 (n = 1) |  |
|  | Cheroki C, 2007 [47] | Cohort | 14 MRKHS II | Submicroscopic genomic imbalances in 1q21.1, 17q12, 22q11.21, and Xq21.31 (n=4) |  |
|  | Cheroki C, 2006 [73] | Cohort | 25 MRKHS individuals | Deletion in 22q11 (excluding WNT-4, RARgamma, RXR-alpha) (n = 1) |  |
|  | Burel A, 2006 [104] | Cohort | 6 MRKHS individuals | No variants of HOXA7-HOXA13 region (n = 6) |  |
|  | Oppelt P, 2005 [17] | Case control | 30 MRKHS and 48 individual controls | AMH promoter sequence variations cannot be the cause of aberrant AMH expression leading to Müllerian duct formation disorders |  |
|  | Clément-Ziza Mi, 2005 [107] | Cohort | 19 MRKHS individuals | No significant variations of WNT4 (n = 19) |  |
|  | Biason-Lauber A, 2004 [77] | Case report | 1 with MRKHS | Variants of the WNT4 (n = 1) |  |
|  | Plevraki E, 2004 [110] | Case series | 6 MRKHS individuals | Positive TSPY gene (n = 2) |  |
|  | Zenteno J C, 2004 [108] | Case control | 15 with Mullerian agenesis and 25 individual controls | No significant difference in Polymorphisms AMH and AMHR genes between MRKHS individuals and controls |  |
|  | Klipstein S, 2003 [109] | Case control | 32 with CUAs  138 controls | GALT enzyme do not affect PMD formation |  |
|  | Timmreck LS, 2003 [92] | Cohort | 25 individuals with CUAs | Variants of CFTR (n = 2) |  |
|  | Aydos S, 2003 [140] | Case report | 1 | Deletion of Xq (n = 1) | MRKHS and gonadal dysgenesis |
|  | Bingham C, 2002 [70] | Cohort | 9 families | Changes in HNF-1beta gene (n = 2 families) | Included those with renal abnormalities and personal or family history of female genital tract malfor-mations, but no history of diabetes |
|  | Resendes D L, 2001 [106] | Case control | 22 with CUAs  96 individual controls | No changes or rare polymorphism in AMH and the AMHR genes (n = 22) |  |
|  | Lindner T H, 1999 [65] | Cohort | 1 family | Deletion in HNF-1beta gene in 4 females. Mullerian aplasia (n=2) | Family with severe genital malformations progressive non-diabetic renal disease and mild DM |
|  | Cramer DW, 1996 [111] | Case control | 13 MRKHS and  their mothers;  113 individual controls | Carriers for the N314D variants of GALT  (n = 6/13 individuals with Müllerian  agenesis and 16/113 individual controls) | Included cases with vaginal agenesis and rudimentary uterus |

[ CES= Cat Eye Syndrome, CUA= Complete Uterine Aplasia]

**2. EXPANDED NAMES FOR GENES**

* CMTM7= CKLF Like MARVEL Transmembrane Domain Containing 7
* MEFV= Familial Mediterranean fever
* IL-32= Interleukin 32
* BAZ2B = Bromodomain Adjacent To Zinc Finger Domain Protein 2B
* KLHL18= Kelch Like Family Member 18
* PIK3CD= Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Delta
* SLC4A10= Solute Carrier Family 4 Member 10
* TNK2= Tyrosine Kinase Non Receptor 2
* PAX= Paired-box gene
* LAMC1= Laminin Subunit Gamma 1
* RARA= Retinoic Acid Receptor Alpha
* HOXA10= Homeobox A10
* SHOX= Short stature Homeobox-containing gene
* MMP14= Matrix Metallopeptidase 14
* LRP10= LDL Receptor Related Protein 10
* IFTP57= Intraflagellar transport protein 57
* HHLA2= Human Endogenous Retrovirus-H Long Terminal Repeat-Associating Protein 2
* MYH15= Myosin Heavy chain 15
* PLA2R1= Phospholipase A2 Receptor 1
* ITGB6= Integrin Subunit Beta 6
* RBMS1= RNA Binding Motif Single Stranded Interacting Protein 1
* FRAS1= Fraser Extracellular Matrix Complex Subunit 1
* CC2D2A= Coiled-Coil And C2 Domain Containing 2A
* KIF14= Kinesin Family Member 14
* RSPO4= R-Spondin 4
* MKKS= McKusick-Kaufman/Bardet-Biedl Syndrome Centrosomal Shuttling Protein
* NPHP3= Nephrocystin 3
* DYNC2H1= Dynein Cytoplasmic 2 Heavy Chain 1
* DOCK4= Dedicator Of Cytokinesis 4
* SPECC1L= Sperm antigen with calponin homology and Coiled-Coil domains 1 Like
* VWF= Von Willebrand Factor
* TBC1D1= TBC1 Domain Family Member 1
* KMT2D= Lysine Methyltransferase 2D
* HOXD3= Homeobox D3
* DLG5= Discs Large MAGUK Scaffold Protein 5
* GLI3= Glioma-Associated Oncogene Family Zinc Finger 3
* HIRA= Histone Cell Cycle Regulator
* GATA= Globin Transcription Factor Binding Protein
* LIFR= Leukemia Inhibitory Factor Receptor Alpha
* CLIP1= CAP-Gly Domain Containing Linker Protein 1
* PRKX= Protein Kinase CAMP-Dependent X-Linked Catalytic Subunit
* MUC1= Mucin 1
* HOXC8= Homeobox C8
* RBM8A= RNA-binding protein 8A
* WNT9B= WNT Family Member 9B
* TBX= T-Box Transcription Factor
* TCF2= Transcription Factor 2; Also called HNF1B
* HNF1B= Hepatocyte Nuclear Factor 1 Homeobox B; Also called TCF2
* ACTR3B= Actin-related protein 3B
* LHX1= LIM Homeobox 1
* WNT= Wingless-related integration site
* GREB1L= Growth Regulation By Estrogen In Breast Cancer 1-Like Protein
* ZNF= Zinc finger protein
* DLGH1= Discs Large Homolog 1
* OXTR= Oxytocin Receptor
* ESR1= Estrogen Receptor 1
* WT1= Wilms Tumor 1
* EMX2= Empty Spiracles Homeobox 2
* WISP2= WNT1 inducible signaling pathway protein 2
* DACT1= Dishevelled Binding Antagonist Of Beta Catenin 1
* HOXA5= Homeobox A5
* HOXA9= Homeobox A9
* TRIM71= tripartite motif containing 71
* CCR4= C‑C motif chemokine receptor 4
* CNOT10= CCR4‑NOT transcription complex subunit 10
* OR1F1= Olfactory receptor family 1 subfamily F member 1
* PBX1= Pre-B-Cell Leukemia Homeobox 1