MUTATIONS SUMMARY

DISEASE NAME	THE MUTATION
T1DM	-Associated with HLA-DR3, DR-4, DQ8(exclusive for DM) - Polymorphism in CTLA4 and PTPN22 genes(common with other autoimmune diseases)
Maturity-onset diabetes of the young (MODY)	germline loss of function mutation in glucokinase (GCK) genes, affects glucose metabolism and insulin secretion
Zollinger Ellison syndrome Gastrinoma	▪ 25% of cases appear as a part of MEN-1 syndrome (multifocal)
▪ Primary adrenal adenoma	PRKAR1A genetic mutation
Adrenal carcinoma	▪ Genetic mutations in: activation of beta-catenin (CTNNB1), inactivation of TP53, MEN1 and PRKAR1A
Primary adrenal hyperplasia	▪ Familial disease: inherited mutation in the tumor suppressor gene: armadillo repeat containing 5 (ARMC5) ▪ Sporadic disease: 50% show ARNC5 mutation, others show ectopic production of G-protein coupled hormone receptors (similar action of ACTH) ▪ Syndromic disease: McCune Albright syndrome, germline activating mutation in GNAS, produces excessive cAMP
Micronodular bilateral adrenal hyperplasia	Two variants: primary pigmented nodular adrenocortical disease or Carney complex (multisystemic disease of endocrine and non-endocrine neoplasms)

	▪ Both variants harbor mutation in cAMP-dependent protein kinase (PRKAR1A gene), producing excessive cAMP
Bilateral idiopathic hyperaldosteronism (60%)	Germline mutation in KCNJ5
Adrenocortical neoplasm (35%)	50% harbor KCNJ5 mutation, which encodes potassium channel on zona granulosa cells (called GIRK4 protein), mutant protein allows influx of sodium and activation of aldosterone synthase enzyme
Familial hyperaldosteronism (5%)	FH-1 is the most common (AKA glucocorticoid-remediable aldosteronism), mutation in CYP11B2 (encoding aldosterone synthase), becomes sensitive to ACTH
CONGENITAL ADRENAL HYPERPLASIA	21-hydroxylase deficiency: the most common deficiency (90%), mutation in CYP21A1 gene
PHEOCHROMOCYTOMA	Genetic mutations in growth-factor receptor pathway genes (RET, NF1) or increased activity of hypoxia-induced transcription factors (HIF-1α , HIF-2α)

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