Supplementary Table S-5. Representative syndromes with hereditary primary excess of hormone over-secreting nodules, adenomas, or cancers. Several other syndromes are described separately as incomplete parts of Supplementary S-1.

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Genes and mutations@</th>
<th>Main hormones</th>
<th>Main tissues over-active</th>
<th>Hyperplastic precursors in tissue</th>
<th>Cause a sporadic neoplasm</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEN1</td>
<td>MEN1-, PTH, Prl, gastrin insulin</td>
<td>Islet*, parathy pituitary</td>
<td>Carcinoid, dermis, adrenal cortex</td>
<td>Su</td>
<td>Y</td>
<td>Marx SJ, Wells SA jr 2011</td>
</tr>
<tr>
<td>MEN4</td>
<td>CDKN1B- (CDKIs) PTH, Prl, gastrin insulin</td>
<td>Islet*, parathy pituitary</td>
<td>Carcinoid, dermis, adrenal cortex</td>
<td>Su</td>
<td>Y</td>
<td>Agarwal SK, Mateo C, et al 2009</td>
</tr>
<tr>
<td>FMTC</td>
<td>RET+ Calcitonin</td>
<td>C-cell</td>
<td></td>
<td></td>
<td></td>
<td>Albores-Saavedra J, Krueger JE 2001</td>
</tr>
<tr>
<td>Gene</td>
<td>Phenotype</td>
<td>Tissue(s)</td>
<td>Adrenomedulla</td>
<td>Paraganglioma</td>
<td>Su</td>
<td>?</td>
</tr>
<tr>
<td>--------</td>
<td>------------</td>
<td>------------------------------------</td>
<td>----------------</td>
<td>---------------</td>
<td>----</td>
<td>---</td>
</tr>
<tr>
<td>DICER1</td>
<td><em>DICER1-</em></td>
<td>ACTH, GH</td>
<td>Thyroid</td>
<td>Lung, kidney sertoli, pineal</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>

& MEN1 and MEN4 are treated as expressing the same or very similar phenotype. Cases of MEN4 are too few and too similar to MEN1, to separate the MEN4 phenotype from MEN1.

*Underlined tissues have high cancer potential (above 5% in adults with tumor of that tissue)

@ Mutation types are: - heterozygous loss of function (inactivation); + heterozygous gain of function (activation).

# Abbreviations: Glucagon cell neoplasia GcGN; Massive macronodular adrenocortical hyperplasia MMAH; Multiple endocrine neoplasia MEN; PRKRA; PRKACA; Familial medullary thyroid cancer FMTC; Von Hippel Lindau Disease VHL; Paraganglioma PGL; Neurofibromatosis type I NF1; Isolated pheochromocytoma IPheo; Hyperparathyroid-Jaw tumor syndrome HPT-JT; Familial isolated pituitary adenoma FIPA; Subtle Su; Yes Y; Parathyroid parathy;

Agarwal SK, Mateo C, Marx SJ 2009 Rare germline mutations in cyclin-dependent kinase inhibitor genes in MEN1 and related states. J Clin Endocrinol Metab/94 1826-34.


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