

Online Resource 1 Custom library used for next generation sequencing (NGS)¹ in our Laboratory, obtained with SureSelect-Custom Hereditary Cancer Solution probes (Agilent, USA). The total coverage was of 77 cancer genes, including the panel of 24 endocrine tumor genes tested in the current research (which are reported in bold type).

Article title: A novel likely pathogenetic variant p.(Cys235Arg) of the *MEN1* gene in multiple endocrine neoplasia type 1 with multifocal glucagonomas

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Gene symbol	Gene name
<i>ACD</i>	ACD shelterin complex subunit and telomerase recruitment factor
<i>AIP</i>	aryl hydrocarbon receptor interacting protein
<i>APC</i>	APC regulator of WNT signaling pathway
<i>ATM</i>	ATM serine/threonine kinase
<i>AXIN2</i>	axin 2
<i>BAP1</i>	BRCA1 associated protein
<i>BARD1</i>	BRCA1 associated RING domain 1
<i>BMPR1A</i>	bone morphogenetic protein receptor type 1A
<i>BRCA1</i>	BRCA1 DNA repair associated
<i>BRCA2</i>	BRCA2 DNA repair associated
<i>BRIP1</i>	BRCA1 interacting helicase 1
<i>CDC73</i>	cell division cycle 73
<i>CDH1</i>	cadherin 1
<i>CDK4</i> (exon 2)	cyclin dependent kinase 4
<i>CDKN1A</i>	cyclin dependent kinase inhibitor 1A
<i>CDKN1B</i>	cyclin dependent kinase inhibitor 1B
<i>CDKN2A</i>	cyclin dependent kinase inhibitor 2A
<i>CDKN2B</i>	cyclin dependent kinase inhibitor 2B
<i>CDKN2C</i>	cyclin dependent kinase inhibitor 2C
<i>CHEK2</i> ²	checkpoint kinase 2
<i>CTR9</i>	CTR9 homolog, Paf1/RNA polymerase II complex component
<i>DICER1</i>	dicer 1, ribonuclease III
<i>DLST</i>	dihydrolipoamide S-succinyltransferase
<i>DNMT3A</i> (exon 8)	DNA methyltransferase 3 alpha
<i>EPCAM</i>	epithelial cell adhesion molecule
<i>FH</i>	fumarate hydratase
<i>FLCN</i>	folliculin
<i>LZTR1</i>	leucine zipper like transcription regulator 1
<i>MAX</i>	MYC associated factor X
<i>MC1R</i>	melanocortin 1 receptor
<i>MDH2</i>	malate dehydrogenase 2
<i>MEN1</i>	menin 1
<i>MET</i> (exons 16 to 19)	MET proto-oncogene, receptor tyrosine kinase
<i>MITF</i> (exon 9)	melanocyte inducing transcription factor
<i>MLH1</i>	mutL homolog 1
<i>MSH2</i>	mutS homolog 2
<i>MSH3</i>	mutS homolog 3
<i>MSH6</i>	mutS homolog 6
<i>MUTYH</i>	mutY DNA glycosylase
<i>NF1</i>	neurofibromin 1
<i>NF2</i>	NF2, moesin-ezrin-radixin like (MERLIN) tumor suppressor
<i>NTHL1</i>	nth like DNA glycosylase 1
<i>PALB2</i>	partner and localizer of BRCA2

<i>PMS2</i> ²	PMS1 homolog 2, mismatch repair system component
<i>POLD1</i> (exons 8 to 13)	DNA polymerase delta 1, catalytic subunit
<i>POLE</i> (exons 9 to 15)	DNA polymerase epsilon, catalytic subunit
<i>POLE2</i> (exons 10 to 17) ²	DNA polymerase epsilon 2, accessory subunit
<i>POT1</i>	protection of telomeres 1
<i>PRKAR1A</i>	protein kinase cAMP-dependent type I regulatory subunit alpha
<i>PTCH1</i>	patched 1
<i>PTCH2</i>	patched 2
<i>PTEN</i> ²	phosphatase and tensin homolog
<i>PTPN11</i>	protein tyrosine phosphatase non-receptor type 11
<i>RAD51C</i>	RAD51 paralog C
<i>RAD51D</i>	RAD51 paralog D
<i>REST</i>	RE1 silencing transcription factor
<i>RET</i>	ret proto-oncogene
<i>RPS20</i>	ribosomal protein S20
<i>SDHA</i> ²	succinate dehydrogenase complex flavoprotein subunit A
<i>SDHAF2</i>	succinate dehydrogenase complex assembly factor 2
<i>SDHB</i>	succinate dehydrogenase complex iron sulfur subunit B
<i>SDHC</i>	succinate dehydrogenase complex subunit C
<i>SDHD</i>	succinate dehydrogenase complex subunit D
<i>SLC25A11</i>	solute carrier family 25 member 11
<i>SMAD4</i>	SMAD family member 4
<i>SMARCA4</i>	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4
<i>SMARCB1</i>	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1
<i>SPRED1</i>	sprouty related EVH1 domain containing 1
<i>STK11</i>	serine/threonine kinase 11
<i>SUFU</i>	SUFU negative regulator of hedgehog signaling
<i>TERF2IP</i>	TERF2 interacting protein
<i>TERT</i> (promoter)	telomerase reverse transcriptase
<i>TMEM127</i>	transmembrane protein 127
<i>TP53</i>	tumor protein p53
<i>TRIM28</i>	tripartite motif containing 28
<i>VHL</i>	von Hippel-Lindau tumor suppressor
<i>WT1</i>	WT1 transcription factor

¹NGS quality parameters: average coverage 1,234x; percentage of bases with at least 20 reads: 100%, percentage of bases with at least 50 reads: 100%; number of reads in regions covered by DNA sequencing: 2,903,124 (mapped reads). Sequencing made with the MiSeq platform (Illumina, San Diego, CA, USA); sequence alignment, variant calling and Copy Number Variants (CNVs) analysis performed with DDM software (Sophia Genetics, Saint Sulpice, Switzerland) (reference genome: GRCh37/hg19 from Genome Reference Consortium), filtering for variant quality, allelic frequency (GnomAD < 0.5% for dominant) and consequence of the substitution.

²The following coding regions were excluded from the deletion/duplication analyses: *CHEK2* exon 7, *POLE2* exon 13, *PTEN* exon 3, *PMS2* exons 12 to 15, *SDHA* exons 13 to 15