Supplementary Information:

Supplementary Methods:

Data on p63 isoforms were obtained from Uniprot [1] and ISOexpresso [2]. Protein sequences were retrieved from Uniprot. Multiple alignments of sequences of p63, p73, and p53 proteins were performed using Clustal Omega implemented in Uniprot [3]. Pairwise sequence alignments of sequence of DNA-binding domain of p63 protein (immunogen of DAK-p63 antibody) and ENNAQTQFSEPQY sequence (immunogen of BC28 antibody) *versu*s p63 isoforms, p73, and p53 proteins were made using Blastp software [4] and EMBL-EBI software [5].

Clinicopathological data of TCGA cohort were downloaded from supplementary files of TCGA publication [6]. Importantly, TCGA cohort was curated for PDAC cases only (n=150) - cases of non-PDAC cancers, as well as normal, pseudo-normal and metastatic samples were excluded [7-9]. Further curation of the database consisted of exclusion of cases in stage IV (distant metastases) (n=4), without data on tumor stage (n=1), and without complete data on progression-free survival (n=6). This resulted in group of n=139 samples. A single case in the cohort was reported in PDAC cohort [6] as grade 4 tumor (TCGA-IB-AAUT-01A). This was a sample of colloid carcinoma; grade in that case was corrected to G1, in accordance with data in cBioportal database and histological picture of the tumor [10]. Data on *TP63*, *TP73*, and *TP53* gene expression were obtained from TSV database [11]. Statistical analysis concerning the relationship between gene expression *versus* clinicopathological variables was based on log2-transformed expression values. Data on overall and progression-free survival were obtained from [8, 9]. Scanned histopathological pictures of TCGA cases were assessed via Cancer Digital Slide Archive [12]. Cutoff Finder [13] was used for the determination of the optimal cut-off value of TP63 expression in curated TCGA cohort.

Data regarding APGI-ICGC cohort was explored using cBioportal [14, 15] and R2 software [16].

Supplementary Figures:

SF 1. Expression of pan-p63 in squamous epithelium of tonsil.

SF 2. Expression of p40 in squamous epithelium of tonsil.

SF 3. Expression of pan-p63 in abluminal cells of minor salivary gland.

SF 4. Expression of p40 in abluminal cells of minor salivary gland.

SF 5. Expression of pan-p63 in lymphoid cells of tonsil.

SF 6. Expression of p40 in lymphoid cells of tonsil.

SF 7. Expression of pan-p63 in fallopian tube.

SF 8. Expression of p40 in fallopian tube.

SF 9. Expression of pan-p63 in normal pancreatic tissue in TMA.

SF 10. Expression of p40 in normal pancreatic tissue in TMA.

SF 11. Undifferentiated carcinoma (anaplastic type). Hematoxylin-eosin stain.

SF 12. Undifferentiated carcinoma with partial rhabdoid growth pattern. Hematoxylin-eosin stain.

SF 13. Undifferentiated carcinoma with osteoclast-like giant cells. Hematoxylin-eosin stain.

SF 14. Expression of pan-p63 in undifferentiated carcinoma (anaplastic type).

SF 15. Expression of pan-p63 in undifferentiated carcinoma (anaplastic type).

SF 16. Expression of p40 in undifferentiated carcinoma (anaplastic type).

SF 17. Expression of p40 in undifferentiated carcinoma (anaplastic type).

SF 18. Expression of p40 in the differentiated component of UCOGC (Abcam antibody).

SF 19. Expression of p40 in the differentiated component of UCOGC (Ventana antibody).

SF 20. Expression of pan-p63 in intraductal papillary mucinous neoplasm.

SF 21. Expression of pan-p63 in mucinous cystic neoplasm.

SF 22. Expression of pan-p63 in mucinous cystic neoplasm.

SF 23. Expression of p40 in mucinous cystic neoplasm.

SF 24. Expression of p40 in mucinous cystic neoplasm.

SF 25. Expression of pan-p63 in pancreatic intraepithelial neoplasia-3.

SF 26. Expression of pan-p63 in pancreatic islets in atrophic parenchyma.

SF 27. Expression of p40 in pancreatic islets in atrophic parenchyma.

SF 28. Expression of pan-p63 in adenosquamous carcinoma in TMA of primary and metastatic ductal carcinomas.

SF 29. Expression of p40 in adenosquamous carcinoma in TMA of primary and metastatic ductal carcinomas.

SF 30. Expression of pan-p63 in ductal adenocarcinoma with micropapillary differentiation in TMA of primary and metastatic ductal carcinomas.

SF 31. Expression of p40 in ductal adenocarcinoma with micropapillary differentiation in TMA of primary and metastatic ductal carcinomas.

SF 32. Expression of pan-p63 in undifferentiated (sarcomatoid) carcinoma in TMA of primary and metastatic ductal carcinomas.

SF 33. Expression of p40 in undifferentiated (sarcomatoid) carcinoma in TMA of primary and metastatic ductal carcinomas.

SF 34. Expression of pan-p63 in conventional ductal adenocarcinoma in TMA of primary and metastatic ductal carcinomas.

SF 35. Expression of p40 in in conventional ductal adenocarcinoma sin TMA of primary and metastatic ductal carcinomas.

SF 36. Expression of pan-p63 in the neuroendocrine tumor in TMA.

SF 37. Expression of p40 in the neuroendocrine tumor in TMA.

SF 38. Expression of pan-p63 in the neuroendocrine carcinoma in TMA.

SF 39. Expression of pan-p63 in the neuroendocrine carcinoma in TMA.

SF 40. Expression of pan-p63 in the neuroendocrine carcinoma with partial squamous differentiation in TMA.

SF 41. Expression of p40 in the neuroendocrine carcinoma in TMA.

SF 42. Expression pf pan-p63 (4A4) in case no. 582 (adenosquamous carcinoma) in Human Protein Atlas resources.

SF 43. Expression pf pan-p63 (4A4) in case no. 646 (ductal adenocarcinoma G1) in Human Protein Atlas resources.

SF 44. Relationship between *TP63* upregulation and overall survival in curated TCGA cohort (n=139).

SF 45. Relationship between *TP63* upregulation and progression-free survival in curated TCGA cohort (n=139).

SF 46. Relationship between *TP63* and *TP73* expression in curated TCGA cohort (n=139).

SF 47. Relationship between *TP63* and *TP53* expression in curated TCGA cohort (n=139).

SF 48. Relationship between histopathological type of tumor versus *TP63* expression in APGI-ICGC cohort.

SF 49. Relationship between tumor grade versus *TP63* expression in APGI-ICGC cohort.

SF 50. Prognostic value of *TP63* expression in APGI-ICGC cohort.

SF 51. Correlation between *TP63* and *TP73* expression in APGI-ICGC cohort.

SF 52. Correlation between *TP63* and *TP53* expression in APGI-ICGC cohort.

Supplementary Data:

Supplementary Data 1. Details of immunohistochemical stains utilized in the study.

Supplementary Data 2. List of p63 isoforms.

Supplementary Data 3. Alignment of protein sequences.

Supplementary Data 4. Potential cross-reactivity of pan-p63/p40 antibodies with p73 and p53 proteins.

Supplementary Data 5. Clinicopathological data of the study cases (undifferentiated carcinomas, n=12).

Supplementary Data 6. The p63 expression in samples of Human Protein Atlas.

Supplementary Data 7. Clinicopathological data of DA cases with *TP63* alterations in TCGA resources.

Supplementary Data 8. Expression of *TP63* isoforms in TCGA cohort.

Supplementary Data 1.

Details of immunohistochemical stains utilized in the study.

Details of immunohistochemical stains utilized in the study.			
Antibody	p63	p40	p40
Manufacturer	Dako/Agilent, Glostrup, Denmark	Ventana, Tucson, AZ, USA	Abcam, Cambridge, UK
Type	mouse monoclonal	mouse monoclonal	mouse monoclonal
Clone	DAK-p63	BC28	BC28 (ab172731)
Immunogen	synthetic peptide derived from the core DNA-binding domain of human p63 protein	synthetic peptide corresponding to human p40 - ΔNp63 amino acids 5-17	synthetic peptide corresponding to human p40 - ΔNp63 amino acids 5-17
Dilution and diluent	prediluted	prediluted	1:100, Antibody diluent, FLEX (Dako)
Antigen retrieval	heat-induced (PT Link Module, Dako), Target Retrieval Solution, pH 9, Dako	heat-induced, Standard CC1, Ventana	heat-induced (PT Link Module, Dako), Target Retrieval Solution, pH 9, Dako
Incubation time	20 minutes	16 minutes	30 minutes
Visualization system	Envision FLEX, Dako	UltraView DAB, Ventana	Envision FLEX+, Dako
IHC machine	Autostainer Link 48, Dako	Benchmark GX, Ventana	Autostainer Link 48, Dako

Supplementary Data 2.

List of p63 isoforms.

List of p63 isoforms.*				
Isoform ID	Uniprot ID	Isoform name	Number of exons	Lenth
uc003fry.2	Q9H3D4-1**	TA*-alpha TAp63α	14	680 aa
uc003frz.2	Q9H3D4-3	TA*-beta TAp63β	13	555 aa
uc003frx.2	Q9H3D4-5	TA*-gamma TAp63ɣ	11	487 aa
uc010hzc.1	Q9H3D4-7	TA*-delta TAp63δ	12	510 aa
	Q9H4D4-9	TA*-epsilon TAp63ε		595 aa
uc003fsc.2	Q9H3D4-2	DeltaN-alpha ΔNp63α	12	586 aa
uc003fsd.2	Q9H3D4-4	DeltaN-beta ΔNp63β	11	461 aa
uc003fsb.2	Q9H3D4-6	DeltaN-gamma ΔNp63ɣ	9	393 aa
	Q9H3D4-8	DeltaN-delta ΔNp63δ		416 aa
uc010hzd.1	Q9H3D4-10	DeltaN-epsilon ΔNp63ε	11	501 aa
	Q9H3D4-11			
	Q9H3D4-12			
uc003fsa.2	C9D7C9		8	
uc003fse.1	C9D7C9		6	

* data taken from Uniprot [1] and ISOexpresso [2], with modification

** Uniprot canonical isoform

Supplementary Data 3. Alignment of protein sequences.

(1) Multiple alignments of protein sequences of p63, p73, and p53 proteins, performed using Clustal Omega. DNA-binding domain of p63 (as defined in Uniprot) written in red; immunogen of BC28 antibody marked in green.

CLUSTAL O(1.2.4) multiple sequence alignment

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SP|Q9H3D4|P63_HUMAN    MNFETSRCATLQYCPDPYIQRFVETPAHFSWKESYYRSTMSQSTQTNEFLSPEVFQHIWD 60
SP|Q9H3D4-2|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-3|P63_HUMAN  MNFETSRCATLQYCPDPYIQRFVETPAHFSWKESYYRSTMSQSTQTNEFLSPEVFQHIWD 60
SP|Q9H3D4-4|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-5|P63_HUMAN  MNFETSRCATLQYCPDPYIQRFVETPAHFSWKESYYRSTMSQSTQTNEFLSPEVFQHIWD 60
SP|Q9H3D4-6|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-7|P63_HUMAN  MNFETSRCATLQYCPDPYIQRFVETPAHFSWKESYYRSTMSQSTQTNEFLSPEVFQHIWD 60
SP|Q9H3D4-8|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-9|P63_HUMAN  MNFETSRCATLQYCPDPYIQRFVETPAHFSWKESYYRSTMSQSTQTNEFLSPEVFQHIWD 60
SP|Q9H3D4-10|P63_HUMAN ------------------------------------------------------------
SP|Q9H3D4-11|P63_HUMAN MNFETSRCATLQYCPDPYIQRFVETPAHFSWKESYYRSTMSQSTQTNEFLSPEVFQHIWD 60
SP|Q9H3D4-12|P63_HUMAN ------------------------------------------------------------
SP|O15350|P73_HUMAN    ---------------------------------------MAQSTAT-SPDGGTTFEHLWS 20
SP|P04637|P53_HUMAN    -----------------------------------MEEPQSDPSVEPPLSQETFSDLWK 24


SP|Q9H3D4|P63_HUMAN    FLEQPICSVQPIDLNFVDEPSEDGATN----KIEISMDCIRMQDSDLSDPMWPQYTNLGL 116
SP|Q9H3D4-2|P63_HUMAN  ------------------------------------MLYLENNAQTQFSEPQYTNLGL 22
SP|Q9H3D4-3|P63_HUMAN  FLEQPICSVQPIDLNFVDEPSEDGATN----KIEISMDCIRMQDSDLSDPMWPQYTNLGL 116
SP|Q9H3D4-4|P63_HUMAN  ------------------------------------MLYLENNAQTQFSEPQYTNLGL 22
SP|Q9H3D4-5|P63_HUMAN  FLEQPICSVQPIDLNFVDEPSEDGATN----KIEISMDCIRMQDSDLSDPMWPQYTNLGL 116
SP|Q9H3D4-6|P63_HUMAN  ------------------------------------MLYLENNAQTQFSEPQYTNLGL 22
SP|Q9H3D4-7|P63_HUMAN  FLEQPICSVQPIDLNFVDEPSEDGATN----KIEISMDCIRMQDSDLSDPMWPQYTNLGL 116
SP|Q9H3D4-8|P63_HUMAN  ------------------------------------MLYLENNAQTQFSEPQYTNLGL 22
SP|Q9H3D4-9|P63_HUMAN  FLEQPICSVQPIDLNFVDEPSEDGATN----KIEISMDCIRMQDSDLSDPMW-------- 108
SP|Q9H3D4-10|P63_HUMAN ------------------------------------------------------------
SP|Q9H3D4-11|P63_HUMAN FLEQPICSVQPIDLNFVDEPSEDGATN----KIEISMDCIRMQDSDLSDPMWPQYTNLGL 116
SP|Q9H3D4-12|P63_HUMAN ------------------------------------MLYLENNAQTQFSEPQYTNLGL 22
SP|O15350|P73_HUMAN    SLEPDST--------YFDLPQSSRGNNEVVGGTDSSMDVFHLEGM-----TTSVMAQFNL 67
SP|P04637|P53_HUMAN    LLPENNVL-SPL-------PS-------------QAMDDLMLSPDDIE--QWFT------ 55


SP|Q9H3D4|P63_HUMAN    LNSMDQQIQNGSSSTSPYNTDHAQNSVT---APSPYAQPSSTFDALSPSPAIPSNTDYPG 173
SP|Q9H3D4-2|P63_HUMAN  LNSMDQQIQNGSSSTSPYNTDHAQNSVT---APSPYAQPSSTFDALSPSPAIPSNTDYPG 79
SP|Q9H3D4-3|P63_HUMAN  LNSMDQQIQNGSSSTSPYNTDHAQNSVT---APSPYAQPSSTFDALSPSPAIPSNTDYPG 173
SP|Q9H3D4-4|P63_HUMAN  LNSMDQQIQNGSSSTSPYNTDHAQNSVT---APSPYAQPSSTFDALSPSPAIPSNTDYPG 79
SP|Q9H3D4-5|P63_HUMAN  LNSMDQQIQNGSSSTSPYNTDHAQNSVT---APSPYAQPSSTFDALSPSPAIPSNTDYPG 173
SP|Q9H3D4-6|P63_HUMAN  LNSMDQQIQNGSSSTSPYNTDHAQNSVT---APSPYAQPSSTFDALSPSPAIPSNTDYPG 79
SP|Q9H3D4-7|P63_HUMAN  LNSMDQQIQNGSSSTSPYNTDHAQNSVT---APSPYAQPSSTFDALSPSPAIPSNTDYPG 173
SP|Q9H3D4-8|P63_HUMAN  LNSMDQQIQNGSSSTSPYNTDHAQNSVT---APSPYAQPSSTFDALSPSPAIPSNTDYPG 79
SP|Q9H3D4-9|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-10|P63_HUMAN ------------------------------------------------------------
SP|Q9H3D4-11|P63_HUMAN LNSMDQQIQNGSSSTSPYNTDHAQNSVT---APSPYAQPSSTFDALSPSPAIPSNTDYPG 173
SP|Q9H3D4-12|P63_HUMAN LNSMDQQIQNGSSSTSPYNTDHAQNSVT---APSPYAQPSSTFDALSPSPAIPSNTDYPG 79
SP|O15350|P73_HUMAN    LSSTMDQMSSRAASASPYTPEHAA-SVP---THSPYAQPSSTFDTMSPAPVIPSNTDYPG 123
SP|P04637|P53_HUMAN    --------EDPGPDEAPRMPEAAPPVAPAPAAPTPAA--PAPAPSWPLSSSVPSQKTYQG 105


SP|Q9H3D4|P63_HUMAN    PHSFDVSFQQSSTAKSATWTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKK 233
SP|Q9H3D4-2|P63_HUMAN  PHSFDVSFQQSSTAKSATWTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKK 139
SP|Q9H3D4-3|P63_HUMAN  PHSFDVSFQQSSTAKSATWTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKK 233
SP|Q9H3D4-4|P63_HUMAN  PHSFDVSFQQSSTAKSATWTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKK 139
SP|Q9H3D4-5|P63_HUMAN  PHSFDVSFQQSSTAKSATWTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKK 233
SP|Q9H3D4-6|P63_HUMAN  PHSFDVSFQQSSTAKSATWTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKK 139
SP|Q9H3D4-7|P63_HUMAN  PHSFDVSFQQSSTAKSATWTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKK 233
SP|Q9H3D4-8|P63_HUMAN  PHSFDVSFQQSSTAKSATWTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKK 139
SP|Q9H3D4-9|P63_HUMAN  --------------------YSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKK 148
SP|Q9H3D4-10|P63_HUMAN ------MLYLENNAQTQFSEYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKK 54
SP|Q9H3D4-11|P63_HUMAN PHSFDVSFQQSSTAKSATWTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKK 233
SP|Q9H3D4-12|P63_HUMAN PHSFDVSFQQSSTAKSATWTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKK 139
SP|O15350|P73_HUMAN    PHHFEVTFQQSSTAKSATWTYSPLLKKLYCQIAKTCPIQIKVSTPPPPGTAIRAMPVYKK 183
SP|P04637|P53_HUMAN    SYGFRLGFLHSGTAKSVTCTYSPALNKMFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQ 165
                                        **  *:*::**:*****:*: * : ** *: :*** :**:8
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SP|Q9H3D4|P63_HUMAN    AEHVTEVVKRCPNHELSREFNEGQIAPPSHLIRVEGNSHAQYVEDPITGRQSVLVPYEPP 293
SP|Q9H3D4-2|P63_HUMAN  AEHVTEVVKRCPNHELSREFNEGQIAPPSHLIRVEGNSHAQYVEDPITGRQSVLVPYEPP 199
SP|Q9H3D4-3|P63_HUMAN  AEHVTEVVKRCPNHELSREFNEGQIAPPSHLIRVEGNSHAQYVEDPITGRQSVLVPYEPP 293
SP|Q9H3D4-4|P63_HUMAN  AEHVTEVVKRCPNHELSREFNEGQIAPPSHLIRVEGNSHAQYVEDPITGRQSVLVPYEPP 199
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SP|Q9H3D4-6|P63_HUMAN  AEHVTEVVKRCPNHELSREFNEGQIAPPSHLIRVEGNSHAQYVEDPITGRQSVLVPYEPP 199
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SP|Q9H3D4-9|P63_HUMAN  AEHVTEVVKRCPNHELSREFNEGQIAPPSHLIRVEGNSHAQYVEDPITGRQSVLVPYEPP 208
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SP|Q9H3D4-11|P63_HUMAN AEHVTEVVKRCPNHELSREFNEGQIAPPSHLIRVEGNSHAQYVEDPITGRQSVLVPYEPP 293
SP|Q9H3D4-12|P63_HUMAN AEHVTEVVKRCPNHELSREFNEGQIAPPSHLIRVEGNSHAQYVEDPITGRQSVLVPYEPP 199
SP|O15350|P73_HUMAN    AEHVTDVVKRCPNHELGRDFNEGQSAPASHLIRVEGNNLSQYVDDPVTGRQSVVVPYEPP 243
SP|P04637|P53_HUMAN    SQHMTEVVRRCPHHERCSD--SDGLAPPQHLIRVEGNLRVEYLDDRNTFRHSVVVPYEPP 223
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SP|O15350|P73_HUMAN    QVGTEFTTILYNFMCNSSCVGGMNRRPILIIITLEMRDGQVLGRRSFEGRICACPGRDRK 303
SP|P04637|P53_HUMAN    EVGSDCTTIHYNYMCNSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACPGRDRR 283
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SP|Q9H3D4-12|P63_HUMAN ADEDSIRKQQVSD--STKNGD----AFRQNTHGIQM--TSIKKRRSPDDELLYLPVRGRE 311
SP|O15350|P73_HUMAN    ADEDHYREQQALNESSAKNGAASKRAFKQSPPAVPALGAGVKKRRHGDEDTYYLQVRGRE 363
SP|P04637|P53_HUMAN    TEEENLRKKGEPHHEL--PPGSTKRALPNNTSS-----SPQPKKKPLDGEYFTLQIRGRE 336
                       ::*:  *::   .             : :.  .     :   *::  * :   * :****

SP|Q9H3D4|P63_HUMAN    TYEMLLKIKESLELMQYLPQHTIETYRQQQ----------QQQHQHLLQKQTSIQSP--- 456
SP|Q9H3D4-2|P63_HUMAN  TYEMLLKIKESLELMQYLPQHTIETYRQQQ----------QQQHQHLLQKQTSIQSP--- 362
SP|Q9H3D4-3|P63_HUMAN  TYEMLLKIKESLELMQYLPQHTIETYRQQQ----------QQQHQHLLQKQTSIQSP--- 456
SP|Q9H3D4-4|P63_HUMAN  TYEMLLKIKESLELMQYLPQHTIETYRQQQ----------QQQHQHLLQKQTSIQSP--- 362
SP|Q9H3D4-5|P63_HUMAN  TYEMLLKIKESLELMQYLPQHTIETYRQQQ----------QQQHQHLLQKHLLSACFRNE 459
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SP|Q9H3D4-7|P63_HUMAN  TYEMLLKIKESLELMQYLPQHTIETYRQQQ----------QQQHQHLLQKQTSIQSP--- 456
SP|Q9H3D4-8|P63_HUMAN  TYEMLLKIKESLELMQYLPQHTIETYRQQQ----------QQQHQHLLQKQTSIQSP--- 362
SP|Q9H3D4-9|P63_HUMAN  TYEMLLKIKESLELMQYLPQHTIETYRQQQ----------QQQHQHLLQKQTSIQSP--- 371
SP|Q9H3D4-10|P63_HUMAN TYEMLLKIKESLELMQYLPQHTIETYRQQQ----------QQQHQHLLQKQTSIQSP--- 277
SP|Q9H3D4-11|P63_HUMAN TYEMLLKIKESLELMQYLPQHTIETYRQQQ----------QQQHQHLLQKQTSIQSP--- 452
SP|Q9H3D4-12|P63_HUMAN TYEMLLKIKESLELMQYLPQHTIETYRQQQ----------QQQHQHLLQKQTSIQSP--- 358
SP|O15350|P73_HUMAN    NFEILMKLKESLELMELVPQPLVDSYRQQQ----------QLLQR-----PSHLQP---- 404
SP|P04637|P53_HUMAN    RFEMFRELNEALELKDAQAGKEPGGSRAHSSHLKSKKGQSTSRHKKLMFKTEGPDSD--- 393
                        :*:: :::*:*** :          * :.             ::

SP|Q9H3D4|P63_HUMAN    -------------SSYGNS-SPPLNKMNSMNKLPSVSQLINPQQRN--ALTPTTIPDGMG 500
SP|Q9H3D4-2|P63_HUMAN  -------------SSYGNS-SPPLNKMNSMNKLPSVSQLINPQQRN--ALTPTTIPDGMG 406
SP|Q9H3D4-3|P63_HUMAN  -------------SSYGNS-SPPLNKMNSMNKLPSVSQLINPQQRN--ALTPTTIPDGMG 500
SP|Q9H3D4-4|P63_HUMAN  -------------SSYGNS-SPPLNKMNSMNKLPSVSQLINPQQRN--ALTPTTIPDGMG 406
SP|Q9H3D4-5|P63_HUMAN  LVEPRRETPKQSDVFFRHS-KPPNRSVYP------------------------------- 487
SP|Q9H3D4-6|P63_HUMAN  LVEPRRETPKQSDVFFRHS-KPPNRSVYP------------------------------- 393
SP|Q9H3D4-7|P63_HUMAN  -------------SSYGNS-SPPLNKMNSMNKLPSVSQLINPQQRN--ALTPTTIPDGMG 500
SP|Q9H3D4-8|P63_HUMAN  -------------SSYGNS-SPPLNKMNSMNKLPSVSQLINPQQRN--ALTPTTIPDGMG 406
SP|Q9H3D4-9|P63_HUMAN  -------------SSYGNS-SPPLNKMNSMNKLPSVSQLINPQQRN--ALTPTTIPDGMG 415
SP|Q9H3D4-10|P63_HUMAN -------------SSYGNS-SPPLNKMNSMNKLPSVSQLINPQQRN--ALTPTTIPDGMG 321
SP|Q9H3D4-11|P63_HUMAN -------------SSYGNS-SPPLNKMNSMNKLPSVSQLINPQQRN--ALTPTTIPDGMG 496
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SP|Q9H3D4-12|P63_HUMAN ----------SSYGNS-SPPLNKMNSMNKLPSVSQLINPQQRN--ALTPTTIPDGMG 402
SP|O15350|P73_HUMAN    ----------PSYGPVLSPMNKVHGGMNKLPSVNQLVGQPPPHSSAATPNLGPVGPG 451
SP|P04637|P53_HUMAN    ------------------------------------------------------------


SP|Q9H3D4|P63_HUMAN    ANIPMMGTHMPMAGDMNGLSPTQALPPPLSMPSTSHCTPPPPYPTDCSIVSFLARLGCSS 560
SP|Q9H3D4-2|P63_HUMAN  ANIPMMGTHMPMAGDMNGLSPTQALPPPLSMPSTSHCTPPPPYPTDCSIVSFLARLGCSS 466
SP|Q9H3D4-3|P63_HUMAN  ANIPMMGTHMPMAGDMNGLSPTQALPPPLSMPSTSHCTPPPPYPTDCSIVRIWQV----- 555
SP|Q9H3D4-4|P63_HUMAN  ANIPMMGTHMPMAGDMNGLSPTQALPPPLSMPSTSHCTPPPPYPTDCSIVRIWQV----- 461
SP|Q9H3D4-5|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-6|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-7|P63_HUMAN  ANRSGKSENP------------------------------------------------- 510
SP|Q9H3D4-8|P63_HUMAN  ANRSGKSENP------------------------------------------------- 416
SP|Q9H3D4-9|P63_HUMAN  ANIPMMGTHMPMAGDMNGLSPTQALPPPLSMPSTSHCTPPPPYPTDCSIVSFLARLGCSS 475
SP|Q9H3D4-10|P63_HUMAN ANIPMMGTHMPMAGDMNGLSPTQALPPPLSMPSTSHCTPPPPYPTDCSIVSFLARLGCSS 381
SP|Q9H3D4-11|P63_HUMAN ANIPMMGTHMPMAGDMNGLSPTQALPPPLSMPSTSHCTPPPPYPTDCSIVSFLARLGCSS 556
SP|Q9H3D4-12|P63_HUMAN ANIPMMGTHMPMAGDMNGLSPTQALPPPLSMPSTSHCTPPPPYPTDCSIVSFLARLGCSS 462
SP|O15350|P73_HUMAN    M-LNNHGHAVPANGEMSSS------HSAQSMVSGSHCTPPPPYHADPSLVSFLTGLGCPN 504
SP|P04637|P53_HUMAN    ------------------------------------------------------------


SP|Q9H3D4|P63_HUMAN    CLDYFTTQGLTTIYQIEHYSMDDLASLKIPEQFRHAIWKGILDHRQLHEFSSPSHLLRTP 620
SP|Q9H3D4-2|P63_HUMAN  CLDYFTTQGLTTIYQIEHYSMDDLASLKIPEQFRHAIWKGILDHRQLHEFSSPSHLLRTP 526
SP|Q9H3D4-3|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-4|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-5|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-6|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-7|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-8|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-9|P63_HUMAN  CLDYFTTQGLTTIYQIEHYSMDDLASLKIPEQFRHAIWKGILDHRQLHEFSSPSHLLRTP 535
SP|Q9H3D4-10|P63_HUMAN CLDYFTTQGLTTIYQIEHYSMDDLASLKIPEQFRHAIWKGILDHRQLHEFSSPSHLLRTP 441
SP|Q9H3D4-11|P63_HUMAN CLDYFTTQGLTTIYQIEHYSMDDLASLKIPEQFRHAIWKGILDHRQLHEFSSPSHLLRTP 616
SP|Q9H3D4-12|P63_HUMAN CLDYFTTQGLTTIYQIEHYSMDDLASLKIPEQFRHAIWKGILDHRQLHEFSSPSHLLRTP 522
SP|O15350|P73_HUMAN    CIEYFTSQGLQSIYHLQNLTIEDLGALKIPEQYRMTIWRGLQDLKQGHDYSTAQQLLRSS 564
SP|P04637|P53_HUMAN    ------------------------------------------------------------


SP|Q9H3D4|P63_HUMAN    SSASTVSVGSSETRGERVIDAVRFTLRQTISFPPR-------DEWNDFNFDMDARRNKQQ 673
SP|Q9H3D4-2|P63_HUMAN  SSASTVSVGSSETRGERVIDAVRFTLRQTISFPPR-------DEWNDFNFDMDARRNKQQ 579
SP|Q9H3D4-3|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-4|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-5|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-6|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-7|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-8|P63_HUMAN  ------------------------------------------------------------
SP|Q9H3D4-9|P63_HUMAN  SSASTVSVGSSETRGERVIDAVRFTLRQTISFPPR-------DEWNDFNFDMDARRNKQQ 588
SP|Q9H3D4-10|P63_HUMAN SSASTVSVGSSETRGERVIDAVRFTLRQTISFPPR-------DEWNDFNFDMDARRNKQQ 494
SP|Q9H3D4-11|P63_HUMAN SSASTVSVGSSETRGERVIDAVRFTLRQTISFPPR-------DEWNDFNFDMDARRNKQQ 669
SP|Q9H3D4-12|P63_HUMAN SSASTVSVGSSETRGERVIDAVRFTLRQTISFPPR-------DEWNDFNFDMDARRNKQQ 575
SP|O15350|P73_HUMAN    NAATISIGGSGELQRQRVMEAVHFRVRHTITIPNRGGPGGGPDEWADFGFDLPDCKARKQ 624
SP|P04637|P53_HUMAN    ------------------------------------------------------------


SP|Q9H3D4|P63_HUMAN    RIKEEGE----- 680
SP|Q9H3D4-2|P63_HUMAN  RIKEEGE----- 586
SP|Q9H3D4-3|P63_HUMAN  ------------
SP|Q9H3D4-4|P63_HUMAN  ------------
SP|Q9H3D4-5|P63_HUMAN  ------------
SP|Q9H3D4-6|P63_HUMAN  ------------
SP|Q9H3D4-7|P63_HUMAN  ------------
SP|Q9H3D4-8|P63_HUMAN  ------------
SP|Q9H3D4-9|P63_HUMAN  RIKEEGE----- 595
SP|Q9H3D4-10|P63_HUMAN RIKEEGE----- 501
SP|Q9H3D4-11|P63_HUMAN RIKEEGE----- 676
SP|Q9H3D4-12|P63_HUMAN RIKEEGE----- 582
SP|O15350|P73_HUMAN    PIKEEFTEAEIH 636
SP|P04637|P53_HUMAN    ------------
```

(2) Results of pairwise alignment of the DNA-binding domain of p63 protein (immunogen of DAK-p63 antibody) *versus* p63 isoforms, as reported by Blastp and EMBOSS Needle:

DNA-binding domain of p63 protein *versus* sequences of p63 isoforms		
p63 isoform	Blastp	EMBOSS Needle (global)
Q9H3D4-1	identities 193/193 (100%) positives 193/193 (100%)	identity: 4/10 (40%) similarity: 6/10 (60%)
Q9H3D4-2	identities 193/193 (100%) positives 193/193 (100%)	identity: 13/13 (100%) similarity: 13/13 (100%)
Q9H3D4-3	identities 193/193 (100%) positives 193/193 (100%)	identity: 4/10 (40%) similarity: 6/10 (60%)
Q9H3D4-4	identities 193/193 (100%) positives 193/193 (100%)	identity: 13/13 (100%) similarity: 13/13 (100%)
Q9H3D4-5	identities 193/193 (100%) positives 193/193 (100%)	identity: 4/10 (40%) similarity: 6/10 (60%)
Q9H3D4-6	identities 193/193 (100%) positives 193/193 (100%)	identity: 13/13 (100%) similarity: 13/13 (100%)
Q9H3D4-7	identities 193/193 (100%) positives 193/193 (100%)	identity: 4/10 (40%) similarity: 6/10 (60%)
Q9H3D4-8	identities 193/193 (100%) positives 193/193 (100%)	identity: 13/13 (100%) similarity: 13/13 (100%)
Q9H3D4-9	identities 174/187 (93%) positives 174/187 (93%)	identity: 4/10 (40%) similarity: 6/10 (60%)
Q9H3D4-10	identities 170/178 (96%) positives (173/178 (97%)	identity: 10/10 (100%) similarity: 10/10 (100%)
Q9H3D4-11	identities 193/193 (100%) positives 193/193 (100%)	identity: 4/10 (40%) similarity: 6/10 (60%)
Q9H3D4-12	identities 193/193 (100%) positives 193/193 (100%)	identity: 13/13 (100%) similarity: 13/13 (100%)

(3) Results of pairwise alignment of the DNA-binding domain of p63 protein (immunogen of DAK-p63 antibody) *versus* both p73 and p53 proteins, as reported by Blastp and EMBOSS Needle:

DNA-binding domain of p63 protein *versus* p73 and p53 proteins		
Protein	Blastp	EMBOSS Needle (global)
p73_HUMAN	identities 165/193 (85%) positives 177/193 (91%)	identity 165/636 (25.9%) similarity 177/636 (27.8%)
p53_HUMAN	identities 109/192 (57%) positives 146/192 (76%)	identity 109/395 (27.6%) similarity 148/395 (37.5%)

(4) Results of pairwise alignment of ENNAQTQFSEPQY sequence (immunogen of BC28 antibody) *versus* isoforms of p63 proteins, as reported by Blastp and EMBOSS Water:

ENNAQTQFSEPQY sequence *versus* sequences of p63 isoforms		
p63 isoform	Blastp	EMBOSS Water (local)
Q9H3D4-1	no significant similarity	identity: 4/10 (40%) similarity: 6/10 (60%)
Q9H3D4-2	identities 13/13 (100%)	identity: 13/13 (100%) similarity: 13/13 (100%)
Q9H3D4-3	no significant similarity	identity: 4/10 (40%) similarity: 6/10 (60%)
Q9H3D4-4	identities 13/13 (100%)	identity: 13/13 (100%) similarity: 13/13 (100%)
Q9H3D4-5	no significant similarity	identity: 4/10 (40%) similarity: 6/10 (60%)
Q9H3D4-6	identities 13/13 (100%)	identity: 13/13 (100%) similarity: 13/13 (100%)
Q9H3D4-7	no significant similarity	identity: 4/10 (40%) similarity: 6/10 (60%)
Q9H3D4-8	identities 13/13 (100%)	identity: 13/13 (100%) similarity: 13/13 (100%)
Q9H3D4-9	no significant similarity	identity: 4/10 (40%) similarity: 6/10 (60%)
Q9H3D4-10	identities 10/10 (100%)	identity: 10/10 (100%) similarity: 10/10 (100%)
Q9H3D4-11	no significant similarity	identity: 4/10 (40%) similarity: 6/10 (60%)
Q9H3D4-12	identities 13/13 (100%)	identity: 13/13 (100%) similarity: 13/13 (100%)

(5) Results of pairwise alignment of ENNAQTQFSEPQY sequence (immunogen of BC28 antibody) *versus* both p73 and p53 proteins, as reported by Blastp and EMBOSS Water:

ENNAQTQFSEPQY sequence (immunogen of BC28 antibody) *versus* p73 and p53 protein		
Protein	Blastp	EMBOSS Water (local)
p73_HUMAN	no significant similarity	identity: 4/7 (57.1%) similarity: 4/7 (57.1%)
p53_HUMAN	no significant similarity	identity: 3/3 (100%) similarity: 3/3 (100%)

Supplementary Data 4.

Potential cross-reactivity of pan-p63/p40 antibodies with p73 and p53 proteins.

To examine potential reactivity of DAK-p63 and BC28 antibodies with p73 protein, a single sample of normal human adult fallopian tube was used [17]. Epithelial cells of the normal human adult fallopian tube should not express p63 [18, 19], in concordance with transcriptomic data [20]. DAK-p63, but not p40 antibodies, showed strong reactivity in a subset of epithelial cells of the fallopian tube (SF 7 and SF 8, respectively). Walthard cell rests were both pan-p63/p40 immunopositive, as expected [18, 19].

To examine potential reactivity of DAK-p63 and BC28 antibodies with p53 protein, 6 UC/UCOGC samples were stained with p53 (DO-7, Dako/Agilent) antibody. Three cases showed nuclear reactivity in 70-80% of cells ("overexpression pattern"). Another 3 cases lacked p53 expression ("null pattern") [21]. Patterns of p53 expression did not overlap with pan-p63/p40 expression, therefore cross-reactivity of DAK-p63 and BC28 antibodies with p53 protein was unlikely.

Supplementary Data 5.

Clinicopathological data of the study cases (undifferentiated carcinomas, n=12).

Clinicopathological data of the study cases (undifferentiated carcinomas, n=12).	
Age (median, range)	63 (41-70)
Sex (Female : Male)	5 : 7
Type of specimens: 1) Resection specimens: Pancreaticoduodenectomy Distal pancreatectomy 2) Incisional biopsy: Primary tumor Secondary deposit	 8/12 4/12 4/12 4/12 2/12 2/12*
Tumour localization: 1) Head 2) Body / tail 3) Not known	 6/12 4/12 2/12
Macroscopical precursor lesion: 1) Mucinous cystic neoplasm 2) Intraductal papillary mucinous neoplasm	 3/8 2/8
Histopathological type of differentiated component: ** 1) DA 2) Adenosquamous carcinomas 3) Colloid carcinoma	 6/9 (four G2 cases and two G3 cases) 2/9 1/9
Histopathological type of dedifferentiated component (based on most predominant component): 1) Undifferentiated carcinoma: Anaplastic ((pleomorphic giant cell) variant Sarcomatoid variant Monomorphic variant 2) Undifferentiated carcinoma with osteoclast-like giant cells	 9/12 4/12 2/12 3/12 3/12
M stage:*** 1) cM0 2) pM1	 11/12 1/12
pN stage (in resected cases):*** pN0 pN1	 5/8 3/8****
pT stage (in resected cases):*** pT3	 8/8
Lymph-vascular invasion (in resected cases)	4/8

Perineural invasion (in resected cases)	5/8
Status of surgical margins (in resected cases): 1) Positive 2) Negative	 2/8 6/8

* metastasis in a peripancreatic lymph node in 1 case, metastases in peripancreatic lymph node and in the liver in 1 case
** detected in 9 cases
*** according to American Joint Committee on Cancer TNM 7th edition (2010)
**** differentiated component in 2 cases, undifferentiated component in 1 case

Supplementary Data 8.

Expression of *TP63* isoforms in TCGA cohort.

Expression of *TP63* isoforms in TCGA cohort.						
Isoform ID	Uniprot ID	Isoform name	Mean expression	Median expression	Minimum expression	Maximum expression
uc003fry.2	Q9H3D4-1**	TA*-alpha TAp63α	11.448	0	0	426.388
uc003frz.2	Q9H3D4-3	TA*-beta TAp63β	8.342	0	0	193.818
uc003frx.2	Q9H3D4-5	TA*-gamma TAp63ɣ	0.596	0	0	6.770
uc010hzc.1	Q9H3D4-7	TA*-delta TAp63δ	5.023	0	0	148.081
	Q9H4D4-9	TA*-epsilon TAp63ε				
uc003fsc.2	Q9H3D4-2	DeltaN-alpha ΔNp63α	28.775	0	0	992.071
uc003fsd.2	Q9H3D4-4	DeltaN-beta ΔNp63β	23.072	0	0	471.975
uc003fsb.2	Q9H3D4-6	DeltaN-gamma ΔNp63ɣ	0.406	0	0	12.315
	Q9H3D4-8	DeltaN-delta ΔNp63δ				
uc010hzd.1	Q9H3D4-10	DeltaN-epsilon ΔNp63ε	74.063	26.675	0	1620.426
	Q9H3D4-11					
	Q9H3D4-12					
uc003fsa.2	C9D7C9		0.074	0	0	3.376
uc003fse.1	C9D7C9		0.607	0	0	14.545

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