

Supplementary Materials: A Novel Nanoproteomic Approach for the Identification of Molecular Targets Associated with Thyroid Tumors

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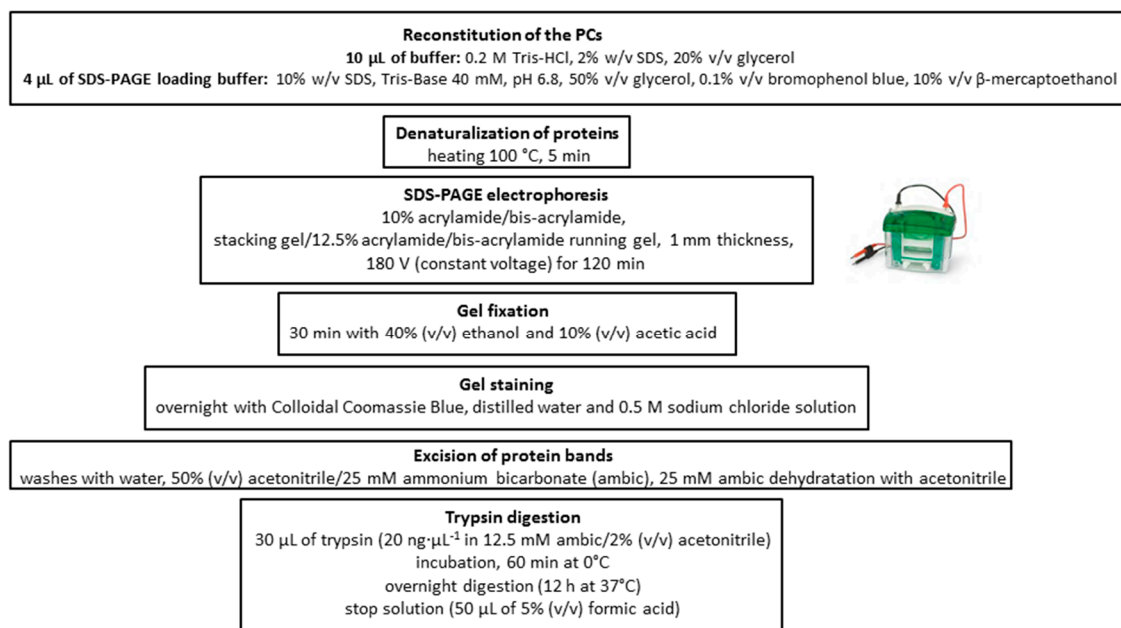
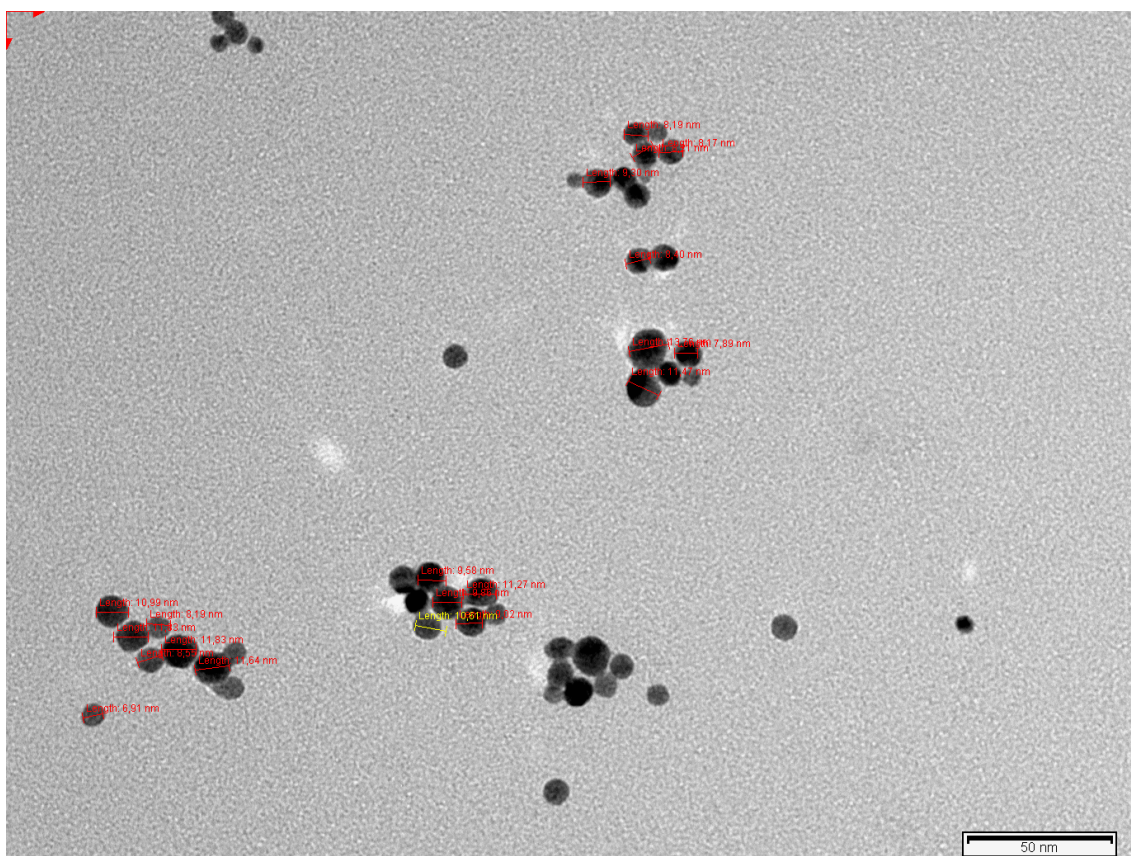


Figure S1. Flowchart depicting the separation by 1D-SDS-PAGE and digestion with trypsin of the corona proteins associated with AgNPs (9.66 ± 1.77), AuNPs (7.55 ± 0.70) and FeNPs (8.25 ± 0.78) previous to the mass spectrometry (LC-MS/MS) identification.

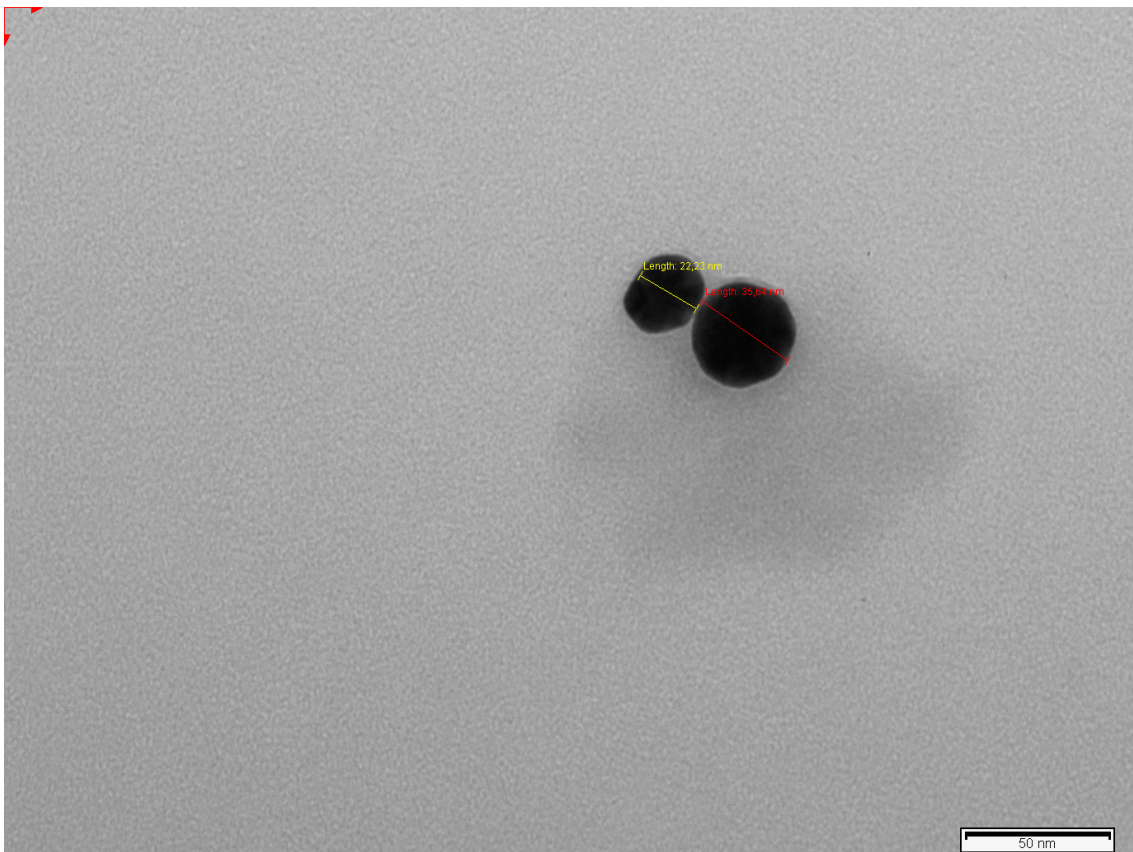
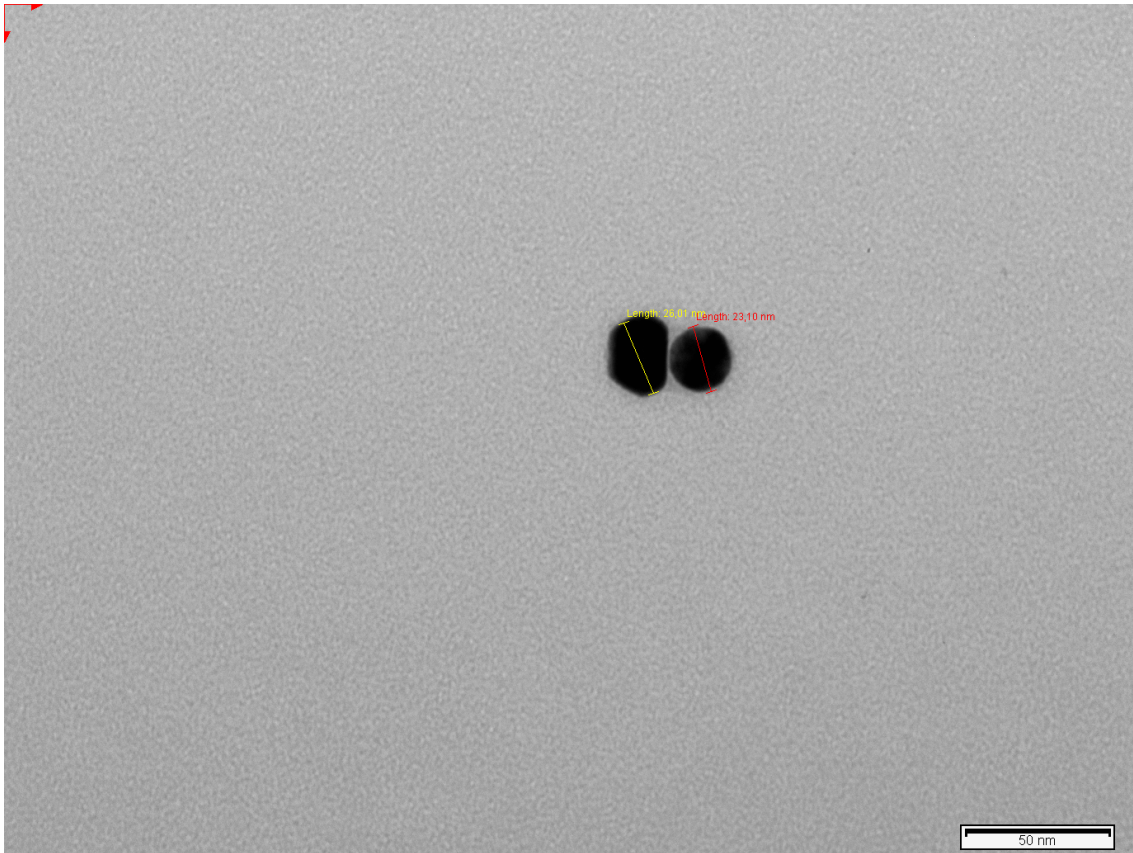
Figure S2. Characterization data and TEM images of a) bare **AgNPs**, b) **Ag@PC controls**: AgNPs after their incubation with pooled tissue extracts of disease-free individuals (controls), and c) **Ag@PC patients**: pooled tissues extracts of patients (diagnosed with FCT) in aqueous phase.

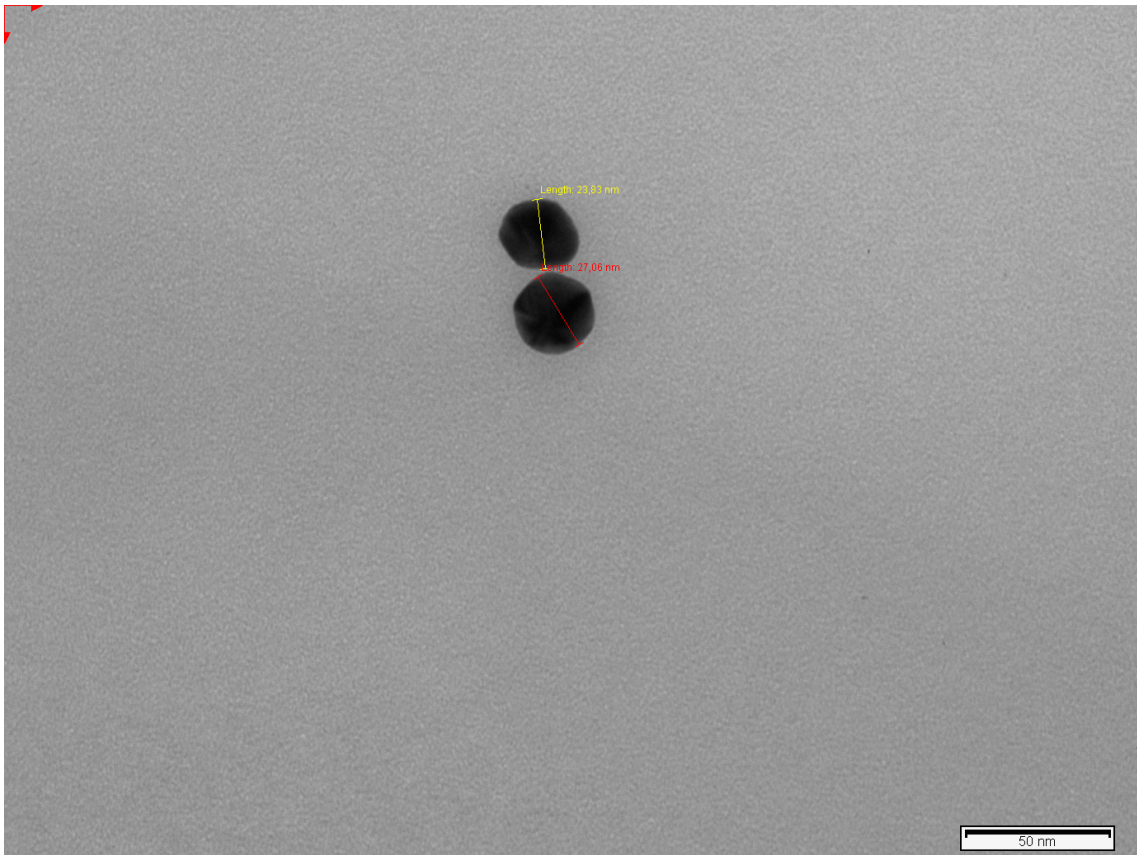
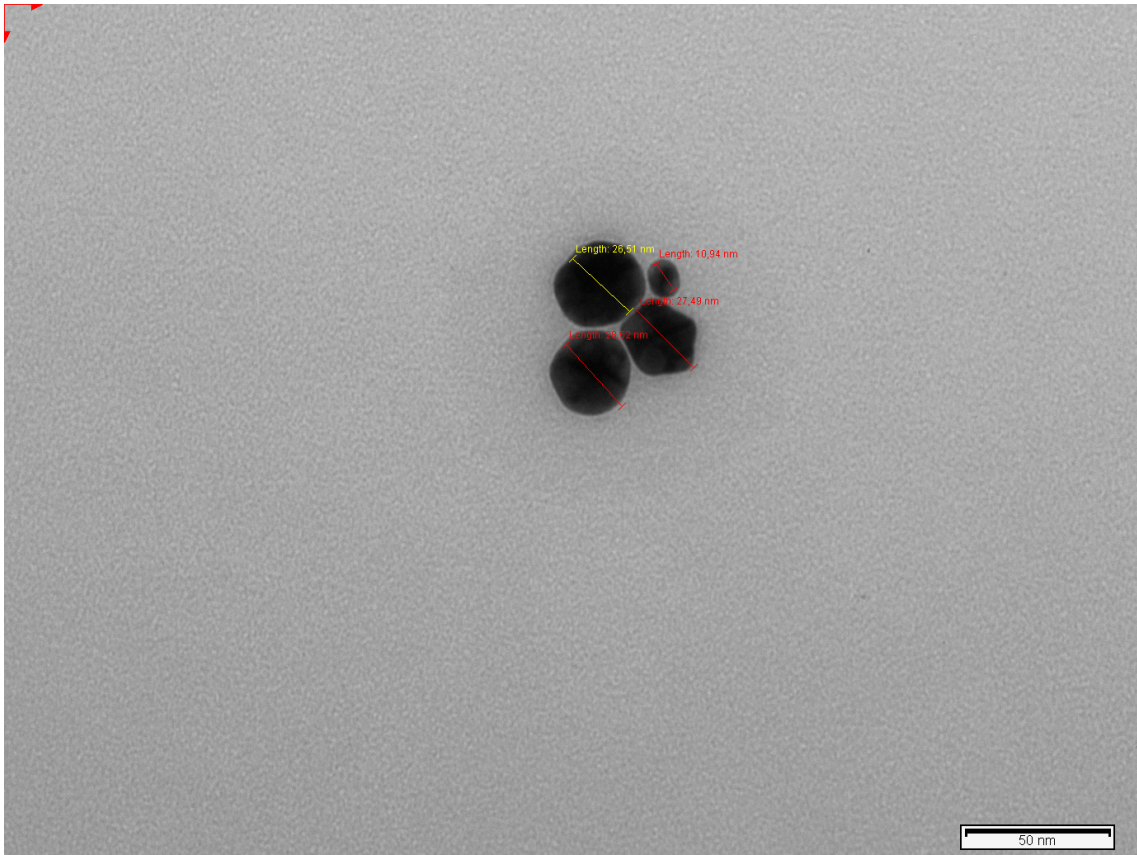
.	AgNPs	Ag@PC controls	Ag@PC patients
1	10.99	26.01	26,71
2	8.19	23.10	35,88
3	11.83	35.33	44,07
4	8.55	26.36	47,10
5	11.83	36.78	33,77
6	11.64	25.76	36,97
7	6.91	32.90	49,56
8	8.19	29.19	35,18
9	8.17	22.23	49,45
10	8.21	15.64	38,06
11	9.30	26.51	20,52
12	8.40	28.52	21,39
13	13.76	27.49	25,36
14	11.47	10.94	30,76
15	7.89	23.83	30,49
16	9.58	27.06	26,01
17	11.27	17.93	46,56
18	9.86	27.71	36,27
19	9.02	35.07	26,02
20	10.61	19.18	45,23
21	13.02	14.14	25,39
22	7.94	18.77	49,31
23	11.17	12.04	32,57
24	9.45	18.14	38,56
25	9.76	27.34	43,42
26	7.50	25.58	28,25
27	12.10	11.35	44,86
28	8.48	10.36	24,53
29	10.48	20.60	47,77
30	10.25	18.30	31,31
31	8.64	15.23	27,19
32	13.49	11.63	34,19
33	10.39	22.96	32,23
34	9.16	20.16	23,95
35	7.89	15.14	38,01
36	8.40	14.96	37,83
37	7.66	11.59	45,14
38	7.18	25.69	20,69
39	8.75	14.98	36,30
40	9.07	34.95	25,63
Count	40	40	40
Mean	9.66	22.03	34.81
Minimum	6.91	10.36	20.52
Maximum	13.76	36.78	49.45
Standard Deviation	1.77	7.53	8.88

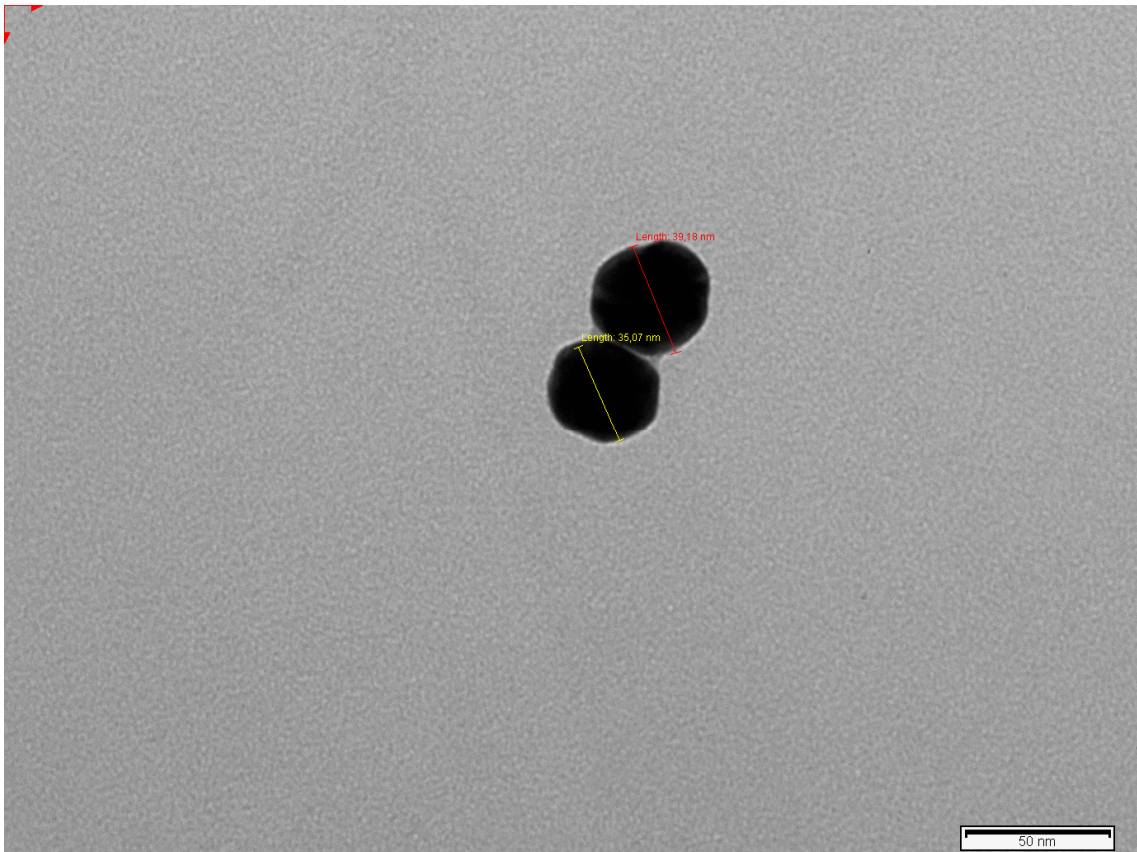
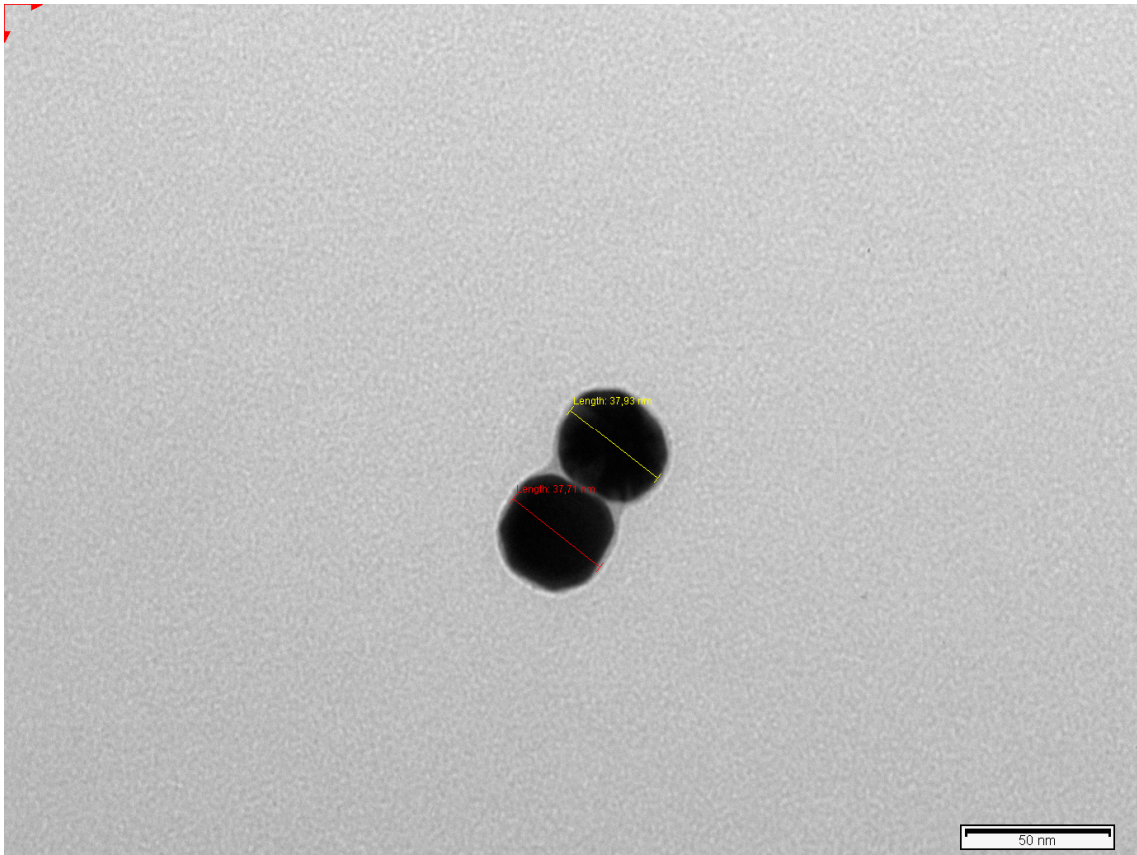
a) TEM image of bare AgNPs in aqueous phase.

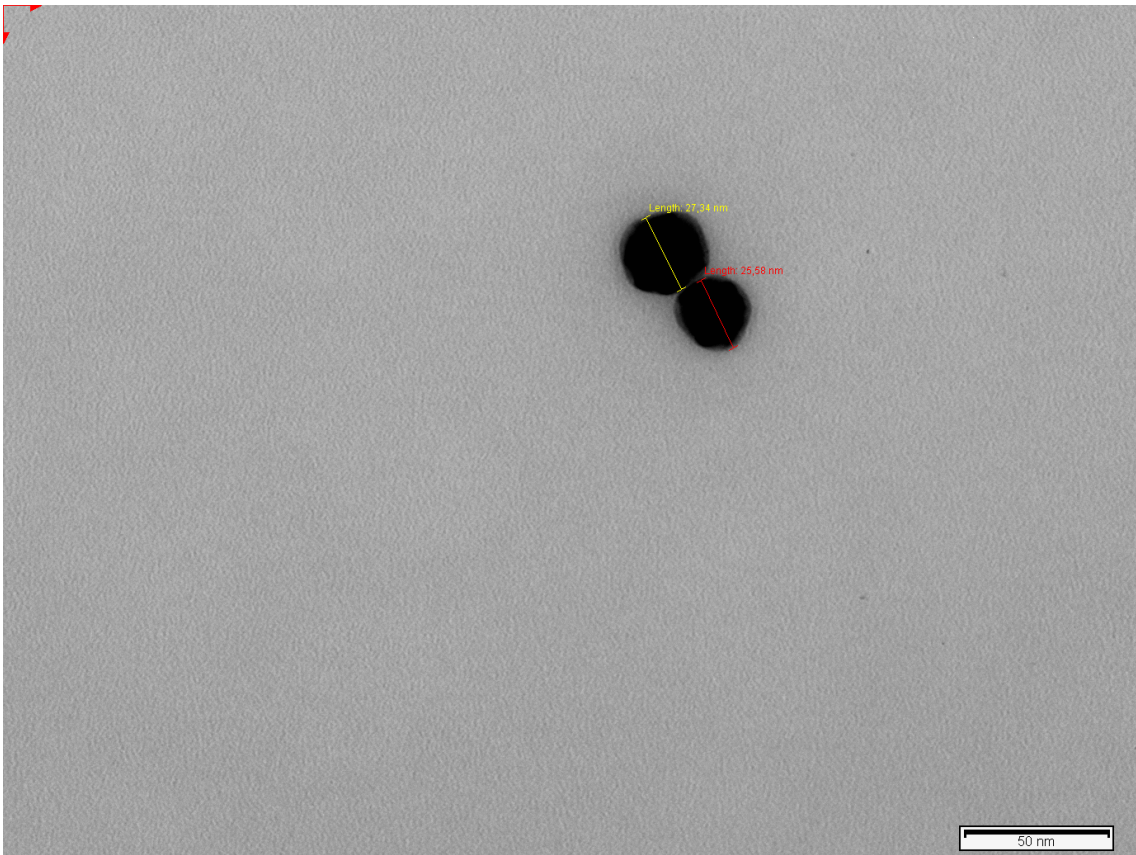
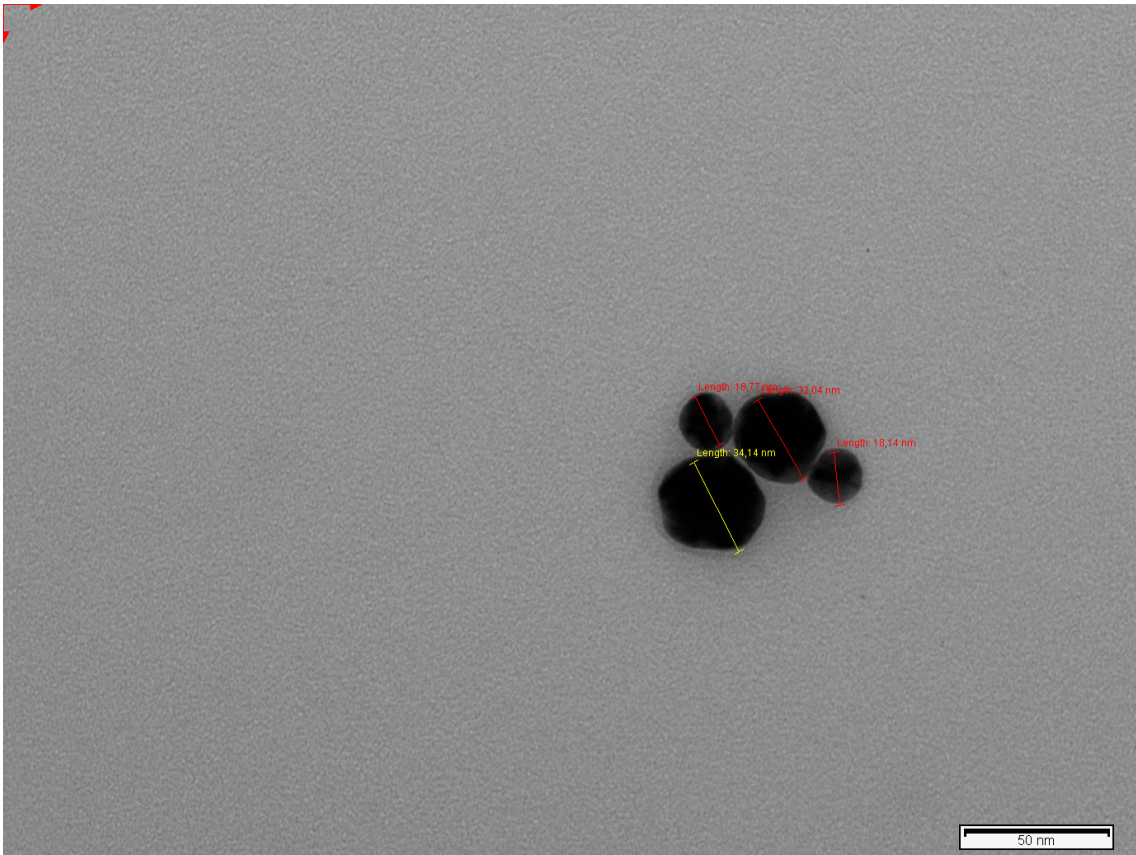


b) TEM images of AgNPs after their incubation with pooled tissue extracts of disease-free individuals (controls) in aqueous phase: AgNPs-controls.









c) TEM images of AgNPs after their incubation with pooled tissue extracts of patients (diagnosed with FCT) in aqueous phase: AgNPs-patients.

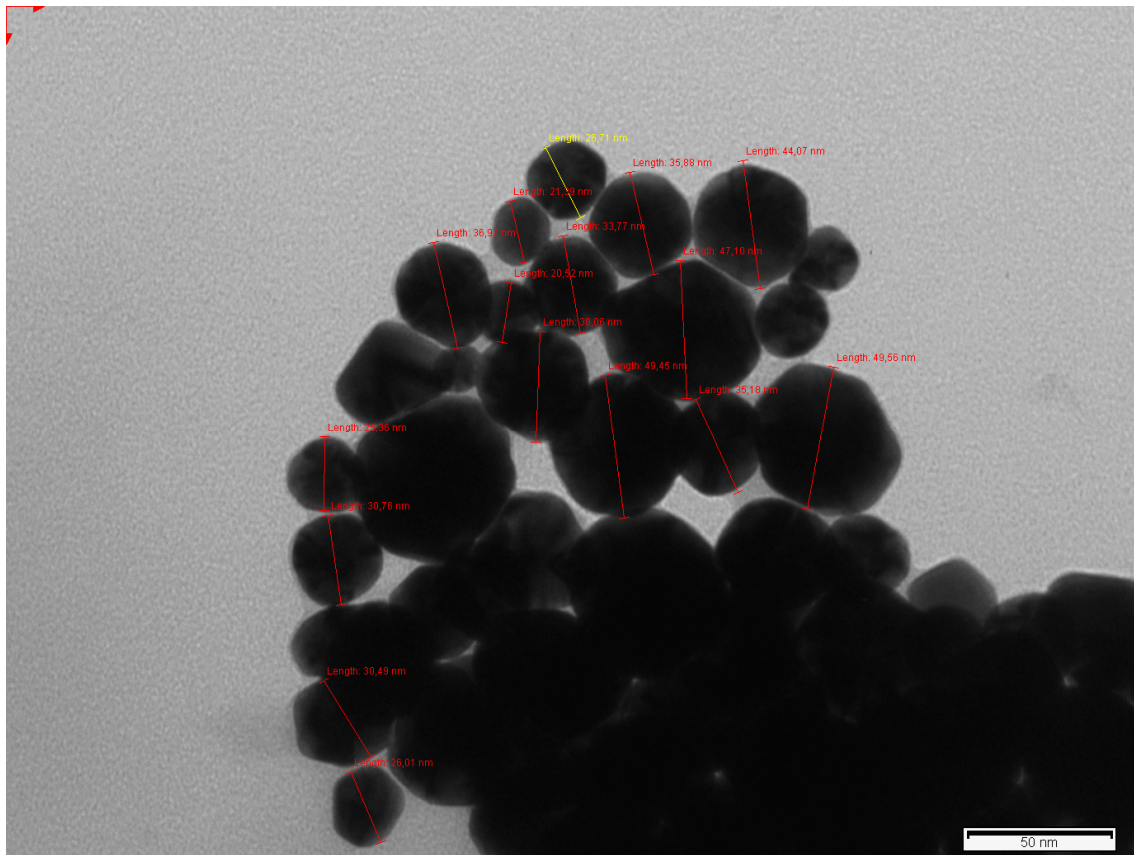
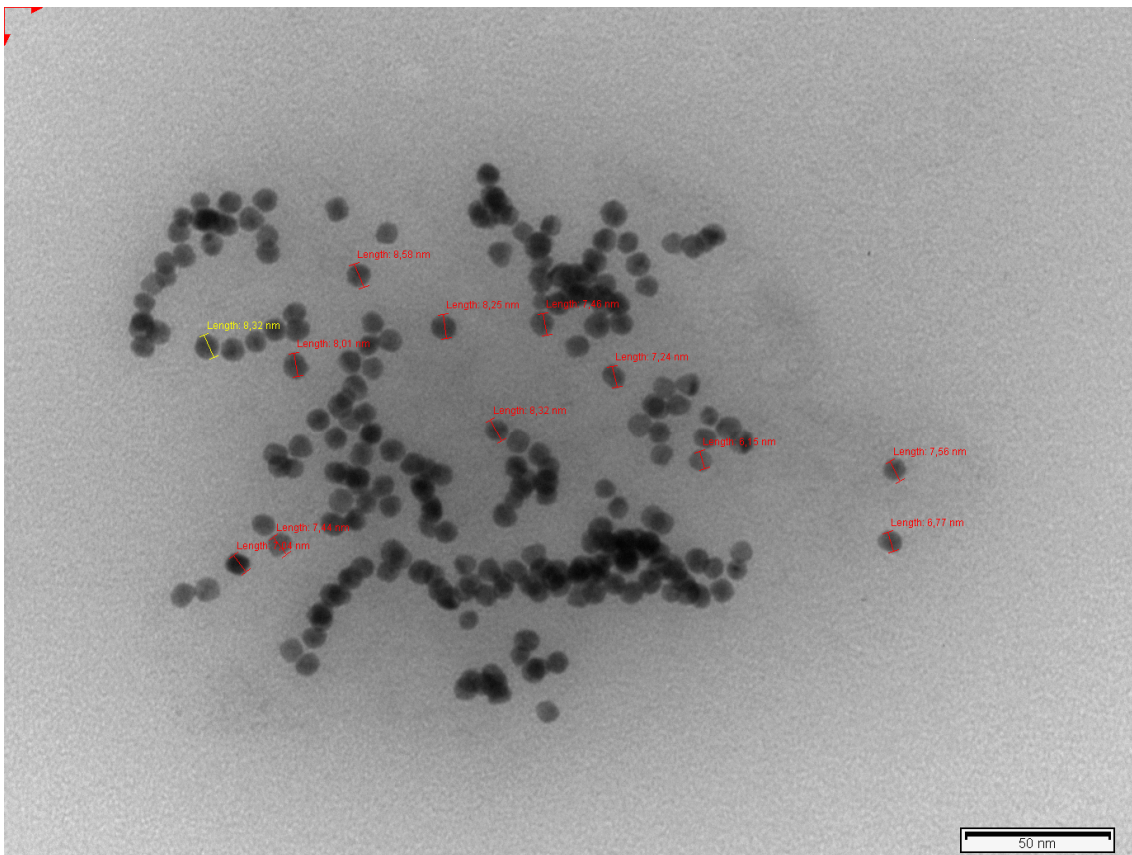


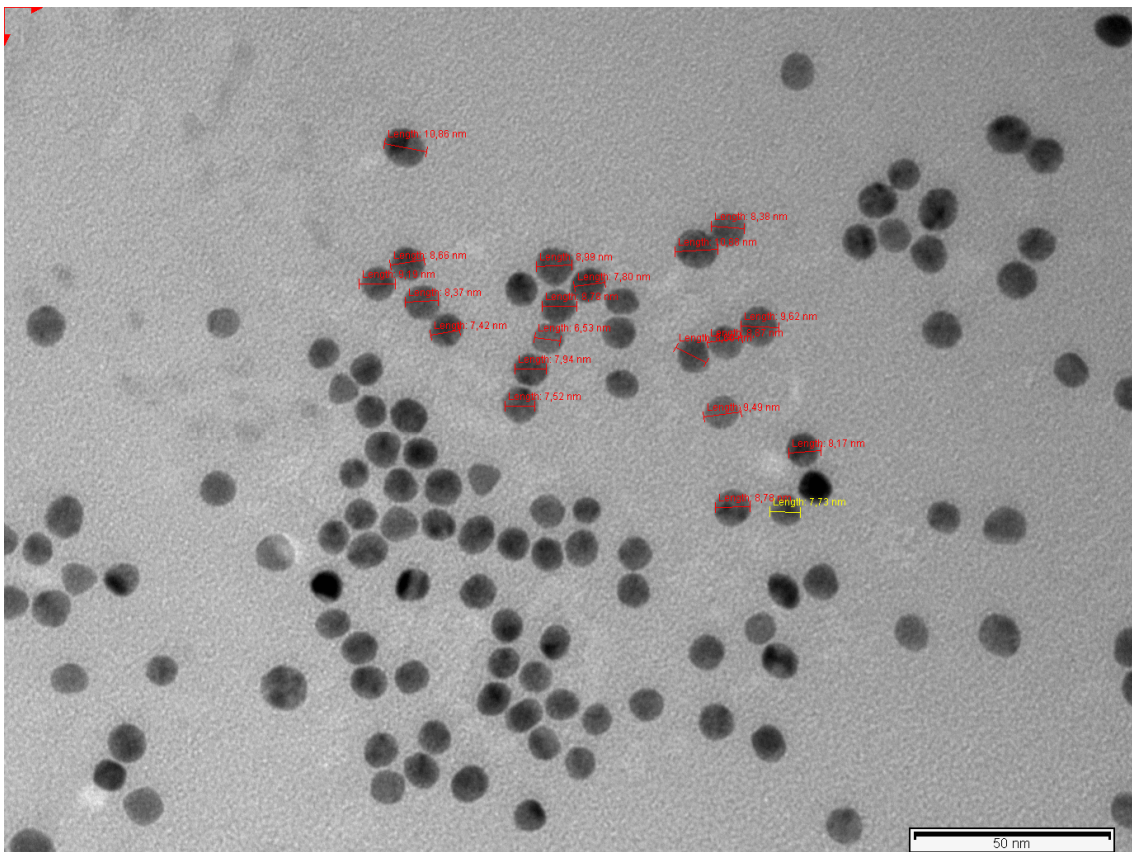
Figure S3. Characterization data and TEM images of a) bare **AuNPs**, b) **Au@PC controls**: AgNPs after their incubation with pooled tissue extracts of disease-free individuals (controls), and c) **Au@PC patients**: pooled tissues extracts of patients (diagnosed with FCT) in aqueous phase.

	AuNPs	Au@PC controls	Au@PC patients
1	7.35	10.86	9.49
2	7.04	8.66	11.50
3	6.33	9.19	10.03
4	6.30	8.37	8.41
5	7.13	7.42	6.95
6	7.13	8.99	9.41
7	7.41	7.80	8.87
8	8.01	8.78	8.57
9	7.74	6.53	9.84
10	8.06	7.94	8.66
11	6.33	7.52	8.82
12	6.70	8.38	7.53
13	7.85	9.88	8.38
14	7.66	9.62	8.90
15	8.07	8.87	10.68
16	8.01	8.60	8.90
17	7.83	9.49	9.44
18	6.58	8.17	9.82
19	7.35	8.78	9.55
20	8.64	7.73	11.48
21	6.58	9.35	9.43
22	8.59	7.89	8.89
23	7.81	8.83	10.13
24	8.01	8.95	9.75
25	8.52	9.95	8.69
26	7.00	10.01	8.26
27	7.98	9.98	10.89
28	6.98	9.95	9.75
29	8.19	8.75	9.64
30	8.68	7.89	8.98
31	6.81	10.11	9.15
32	7.39	9.73	10.06
33	6.82	10.98	8.96
34	7.44	9.01	8.88
35	8.19	8.98	9.23
36	8.58	8.63	9.56
37	7.39	9.63	8.76
38	8.84	8.22	8.36
39	7.17	10.15	10.02
40	7.59	9.86	9.35
Count	40	40	40
Mean	7.55	8.96	9.29
Minimum	6.30	7.42	7.53
Maximum	8.84	10.86	11.50
Standard Deviation	0.70	0.97	0.91

a) bare AuNPs in aqueous phase.



b) TEM images of AuNPs after their incubation with pooled tissue extracts of disease-free individuals (controls) in aqueous phase: AuNPs-controls.



c) TEM images of AuNPs after their incubation with pooled tissue extracts of patients (diagnosed with FCT) in aqueous phase: AuNPs-patients.

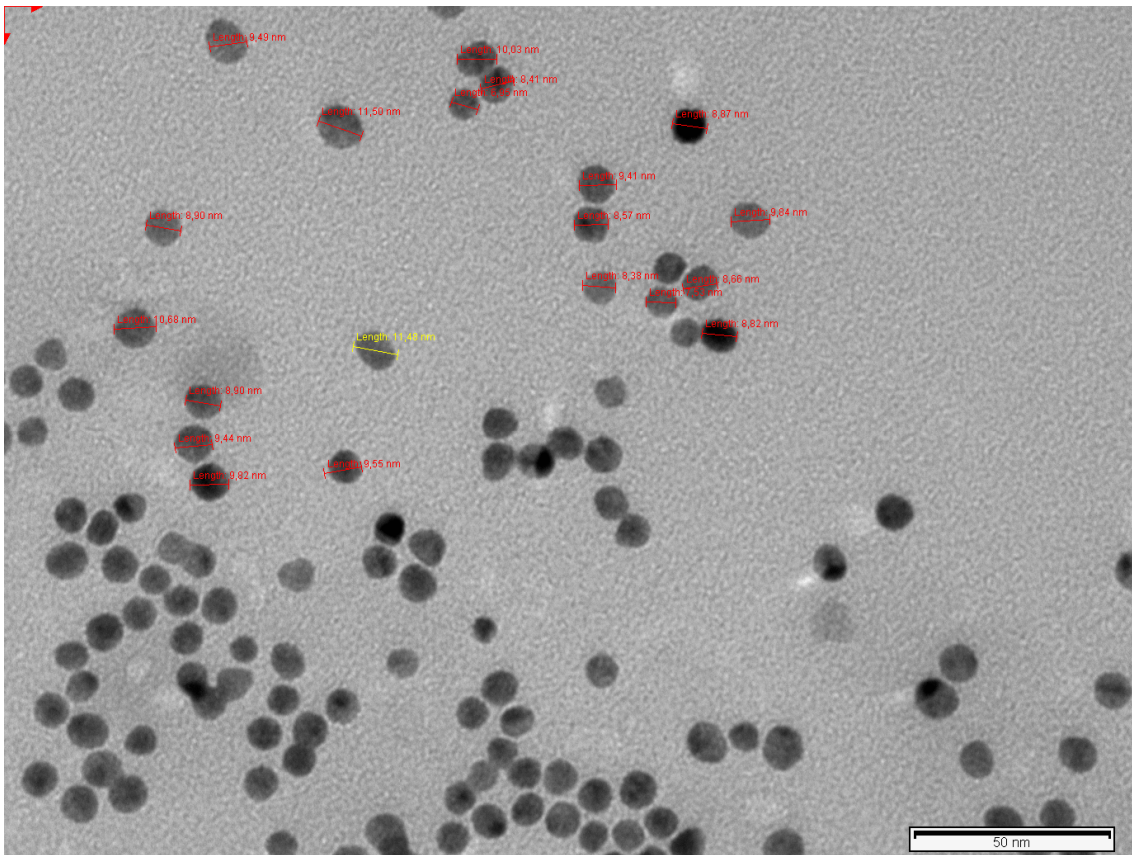
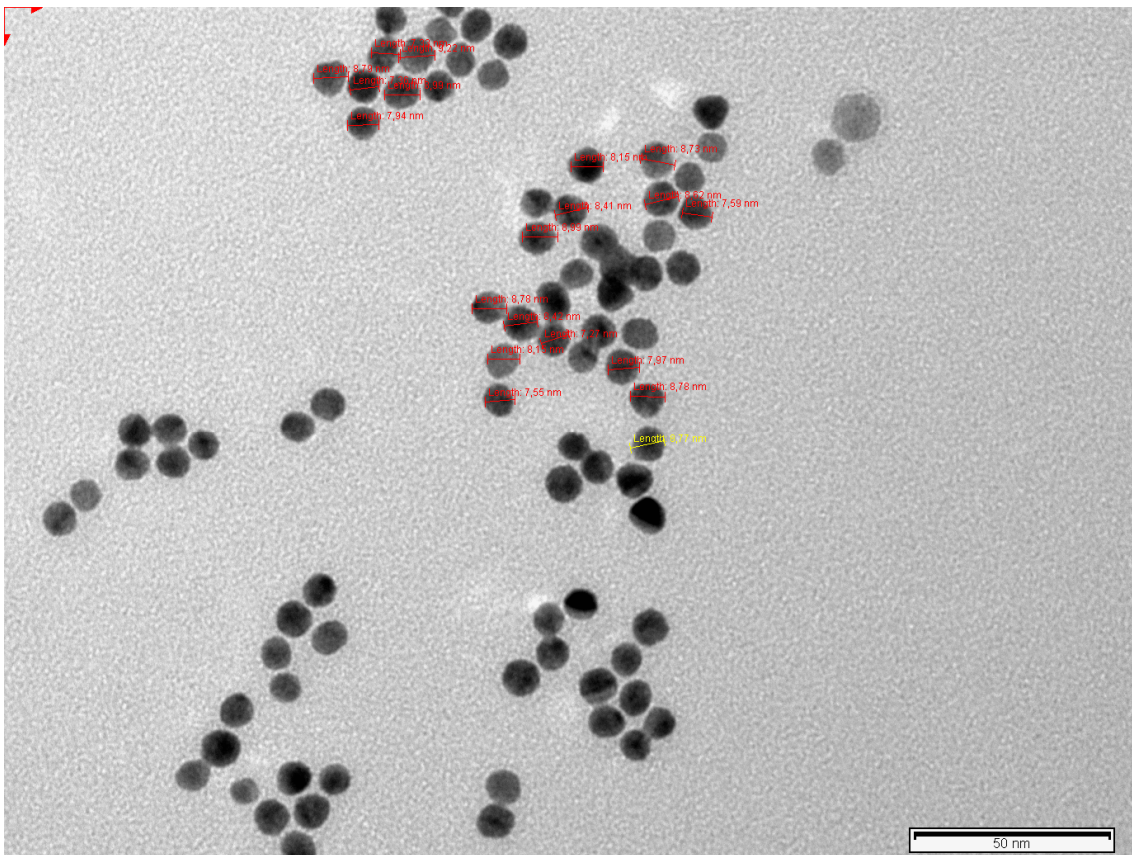


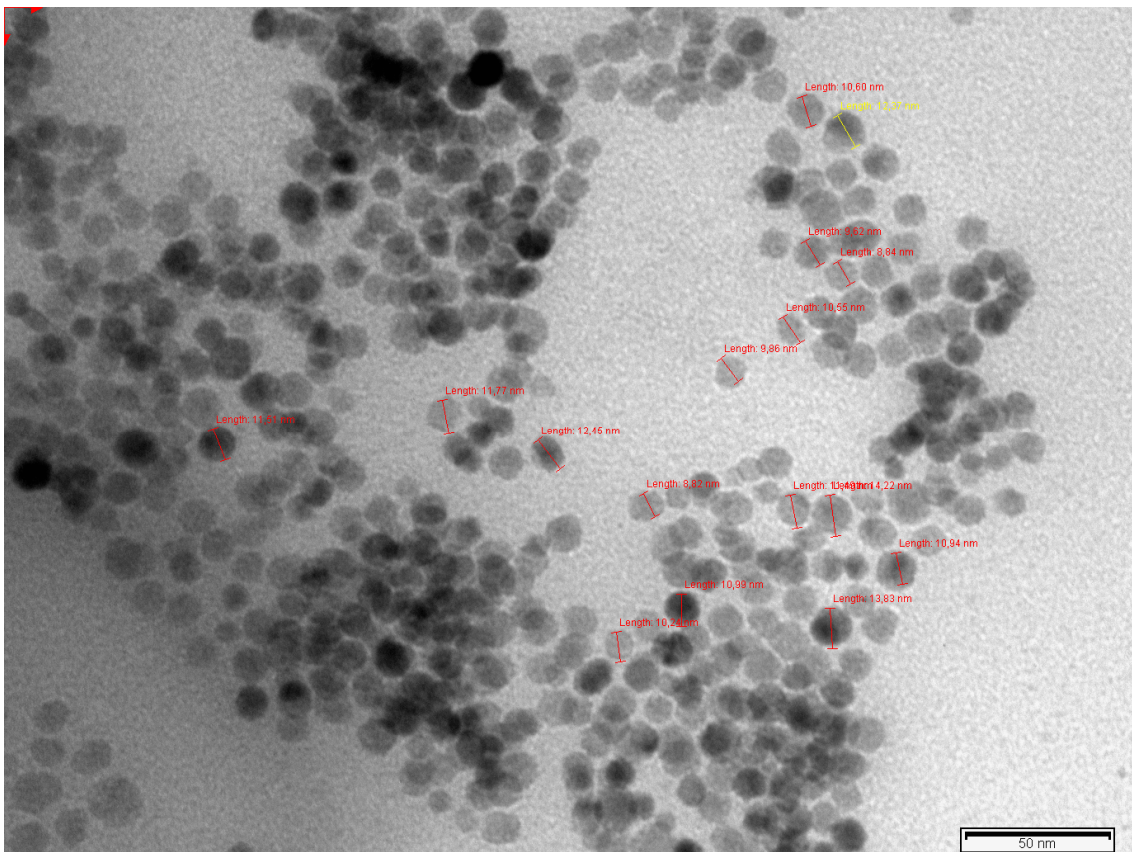
Figure 4. Characterization data and TEM images of a) bare FeNPs, b) Fe@PC controls: AgNPs after their incubation with pooled tissue extracts of disease-free individuals (controls), and c) Fe@PC patients: pooled tissues extracts of patients (diagnosed with FCT) in aqueous phase.

	FeNPs	Fe@PC controls	Fe@PC patients
1	7.33	9.64	12.28
2	9.22	12.63	8.95
3	8.79	10.21	10.99
4	7.36	12.86	11.27
5	8.99	8.40	12.19
6	7.94	14.88	14.11
7	8.15	8.95	13.92
8	8.73	12.85	10.63
9	8.62	11.17	9.30
10	7.59	11.00	10.60
11	8.41	11.07	10.71
12	8.99	12.87	10.73
13	8.78	12.56	13.63
14	8.42	14.12	14.49
15	7.27	9.69	11.31
16	7.97	13.57	13.11
17	8.78	10.25	13.76
18	8.15	11.89	12.55
19	7.55	14.43	14.24
20	8.77	8.32	11.85
21	8.87	12.10	13.07
22	9.07	11.44	10.96
23	6.07	9.99	13.48
24	8.80	10.18	11.02
25	8.15	9.60	9.62
26	6.27	12.37	11.96
27	9.82	10.60	10.21
28	7.52	9.62	9.58
29	9.42	8.84	9.92
30	8.57	10.55	11.51
31	8.36	9.86	9.96
32	8.42	8.82	10.48
33	8.15	11.49	9.58
34	7.95	14.22	13.81
35	8.59	10.94	12.17
36	7.46	13.83	11.22
37	8.36	10.99	9.96
38	8.15	10.24	10.43
39	7.34	11.77	11.22
40	8.78	12.45	12.14
Count	40	40	40
Mean	8.25	11.28	11.57
Minimum	6.27	8.32	8.95
Maximum	9.22	14.88	14.24
Standar Deviation	0.78	1.76	1.54

a) bare FeNPs in aqueous phase.



b) TEM images of AgNPs after their incubation with pooled tissue extracts of disease-free individuals (controls) in aqueous phase: FeNPs-controls.



c) TEM images of FeNPs after their incubation with pooled tissue extracts of patients (diagnosed with FCT) in aqueous phase: FeNPs-patients.

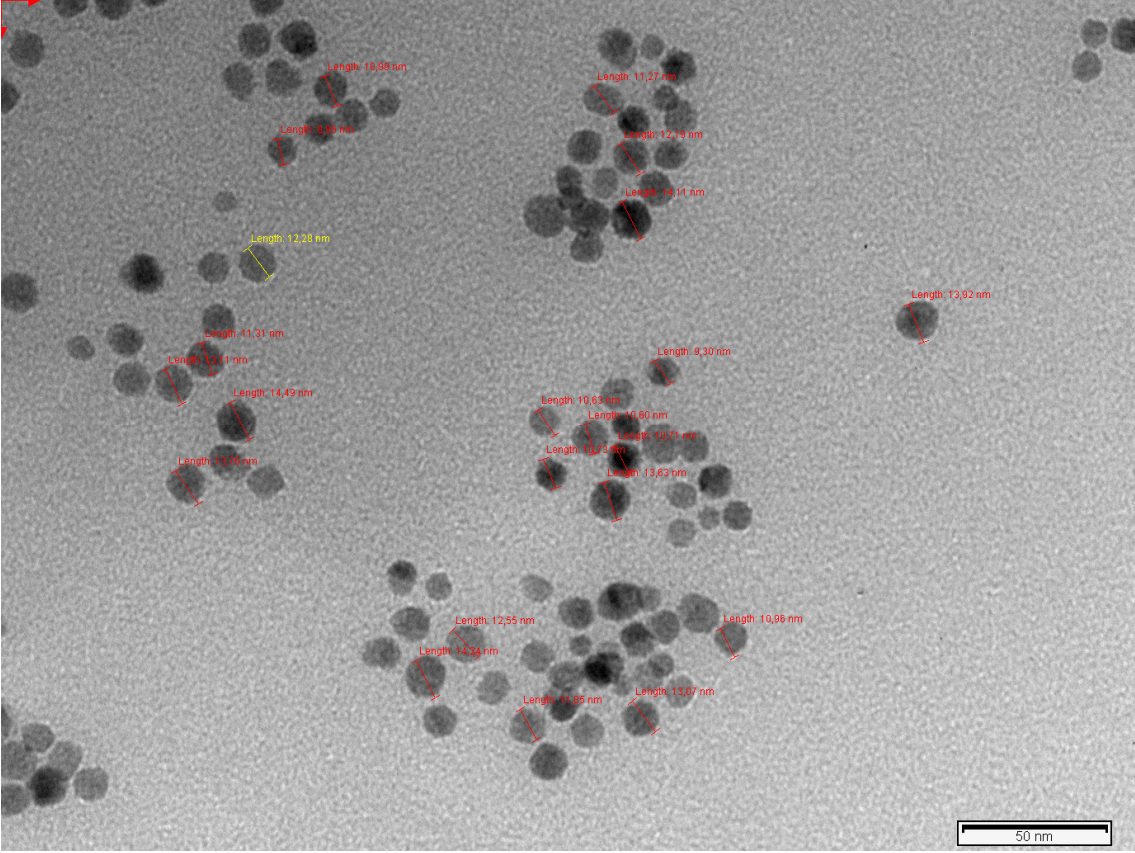


Figure S5. Venn diagrams representing the number of shared and specific molecular targets identified for the different tumor thyroid malignancies (FTA, FTC, CV-PTC and FV-PTC).

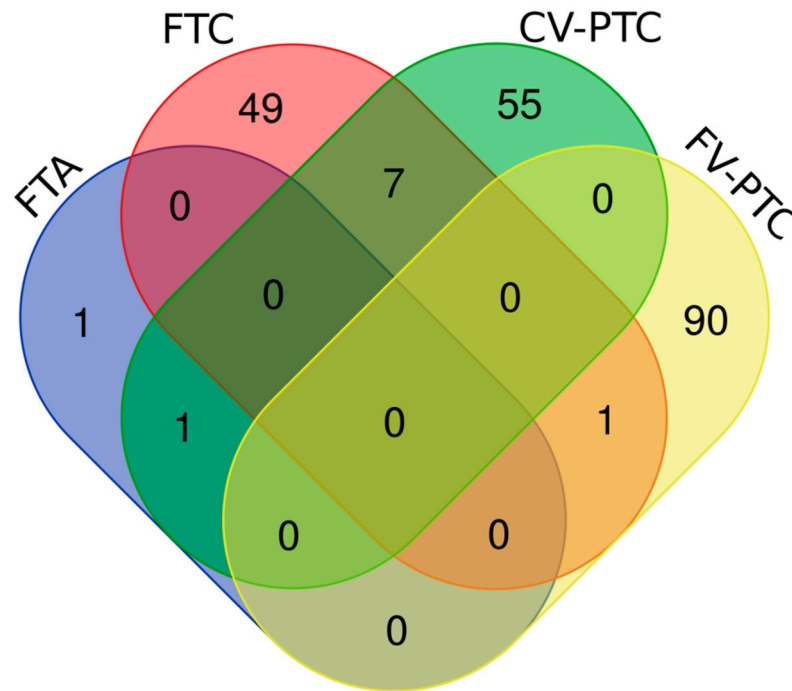


Figure S6. Classification according to the **molecular function** of the potential molecular targets identified in patients with FTA and patients with different types of thyroid cancers (FTC, CV-PTC and FV-PTC). The percentage in each category is the ratio between the number of proteins in each category and total proteins identified in that fraction.

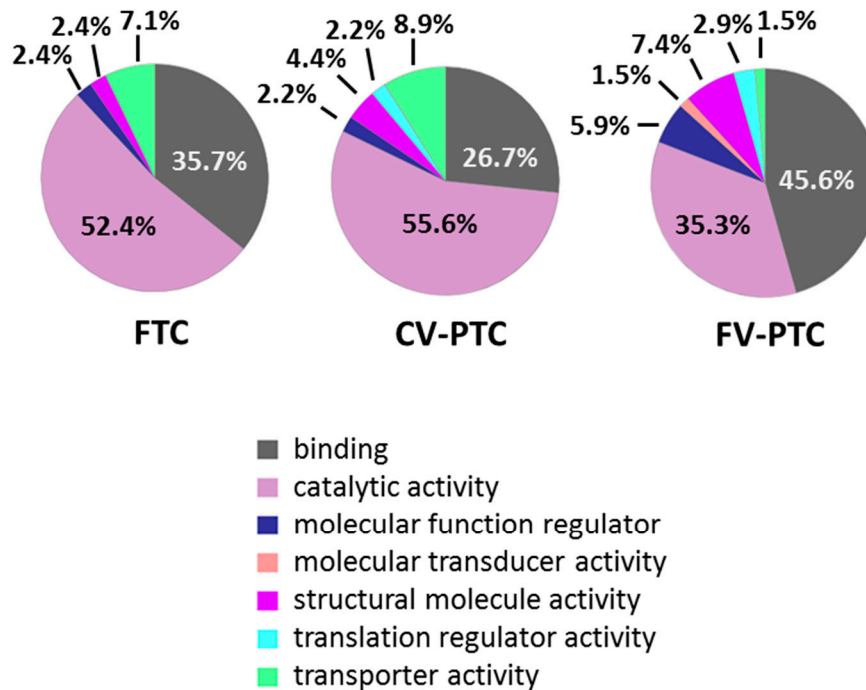
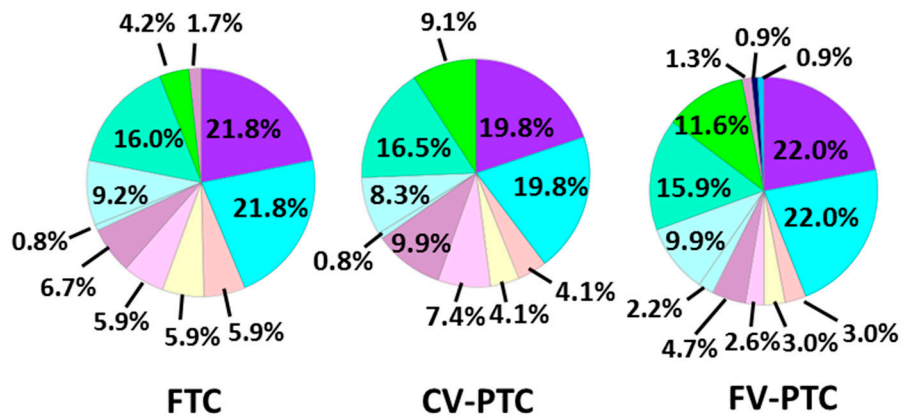


Figure S7. Classification according to the **cellular component** of the potential molecular targets in patients with FTA and patients with different types of thyroid cancers (FTC, CV-PTC and FV-PTC). The percentage in each category is the ratio between the number of proteins in each category and total proteins identified in that fraction.



- cell part
- cell
- extracellular region part
- extracellular region
- membrane part
- membrane
- membrane-enclosed lumen
- organelle part
- organelle
- protein-containing complex
- supramolecular complex
- synapse part
- synapse

Figure S8. Classification according to the **biological process** of the potential molecular targets identified in patients with FTA and patients with different types of thyroid cancers (FTC, CV-PTC and FV-PTC). The percentage in each category is the ratio between the number of proteins in each category and total proteins identified in that fraction.

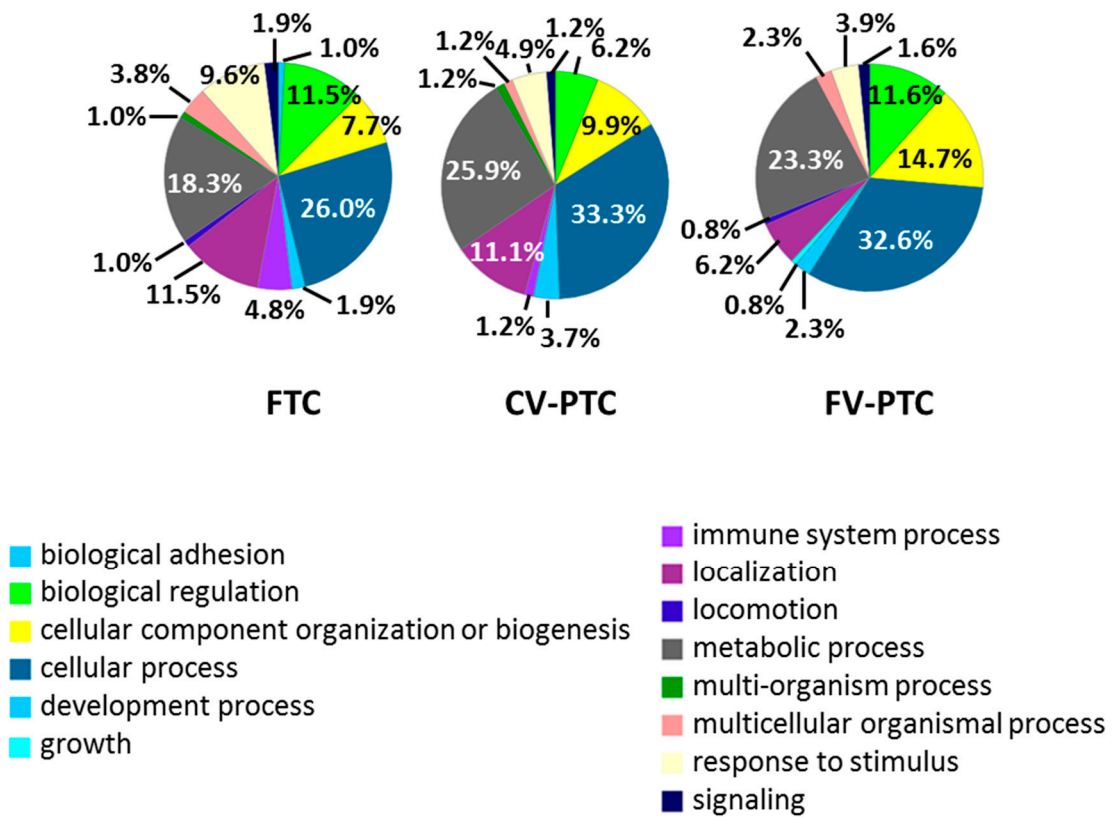
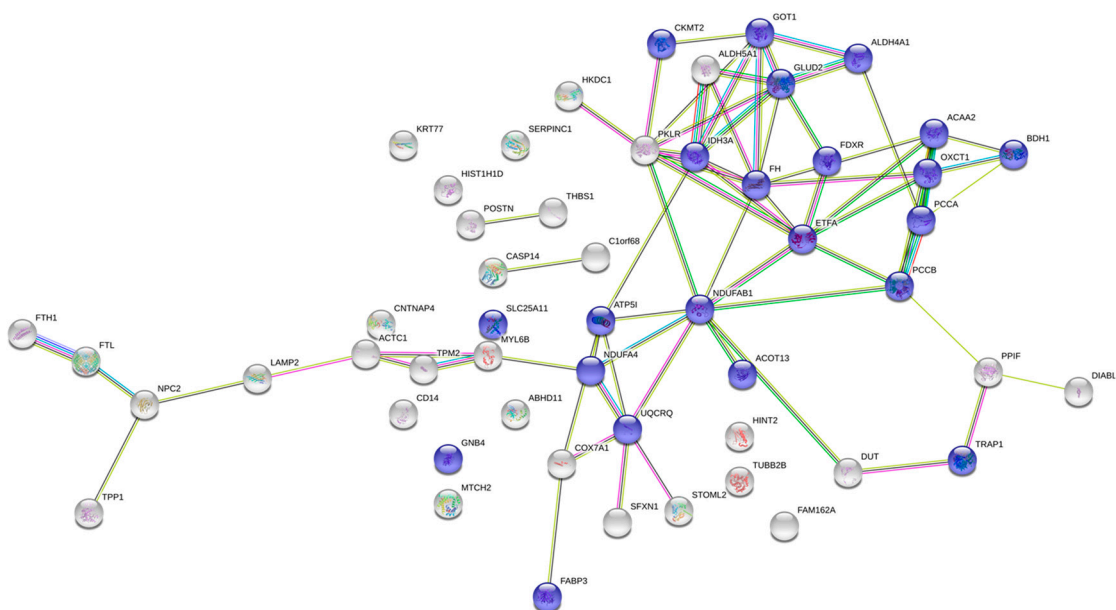
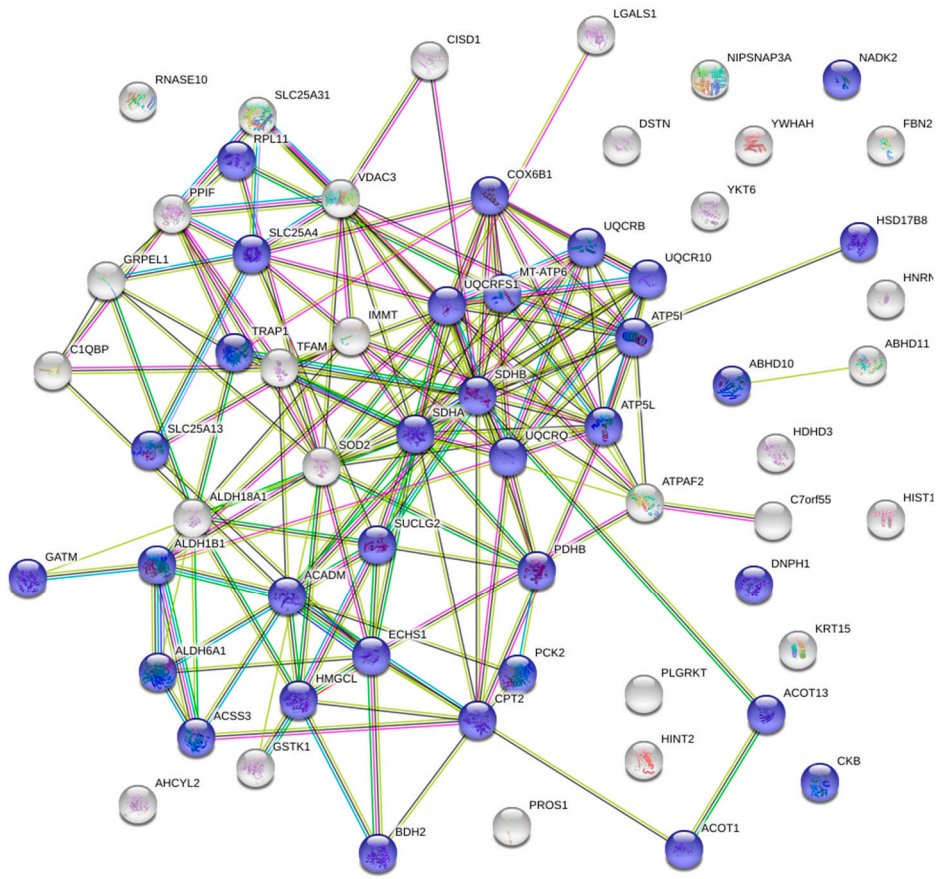


Figure S9. Significant clusters that contain terms and pathways related to the metabolic reorganization in the FTC (A), CV-PTC (B) and FV-PTC (C) PPI network analysis using the STRING v.10.0 database.

A



B



C

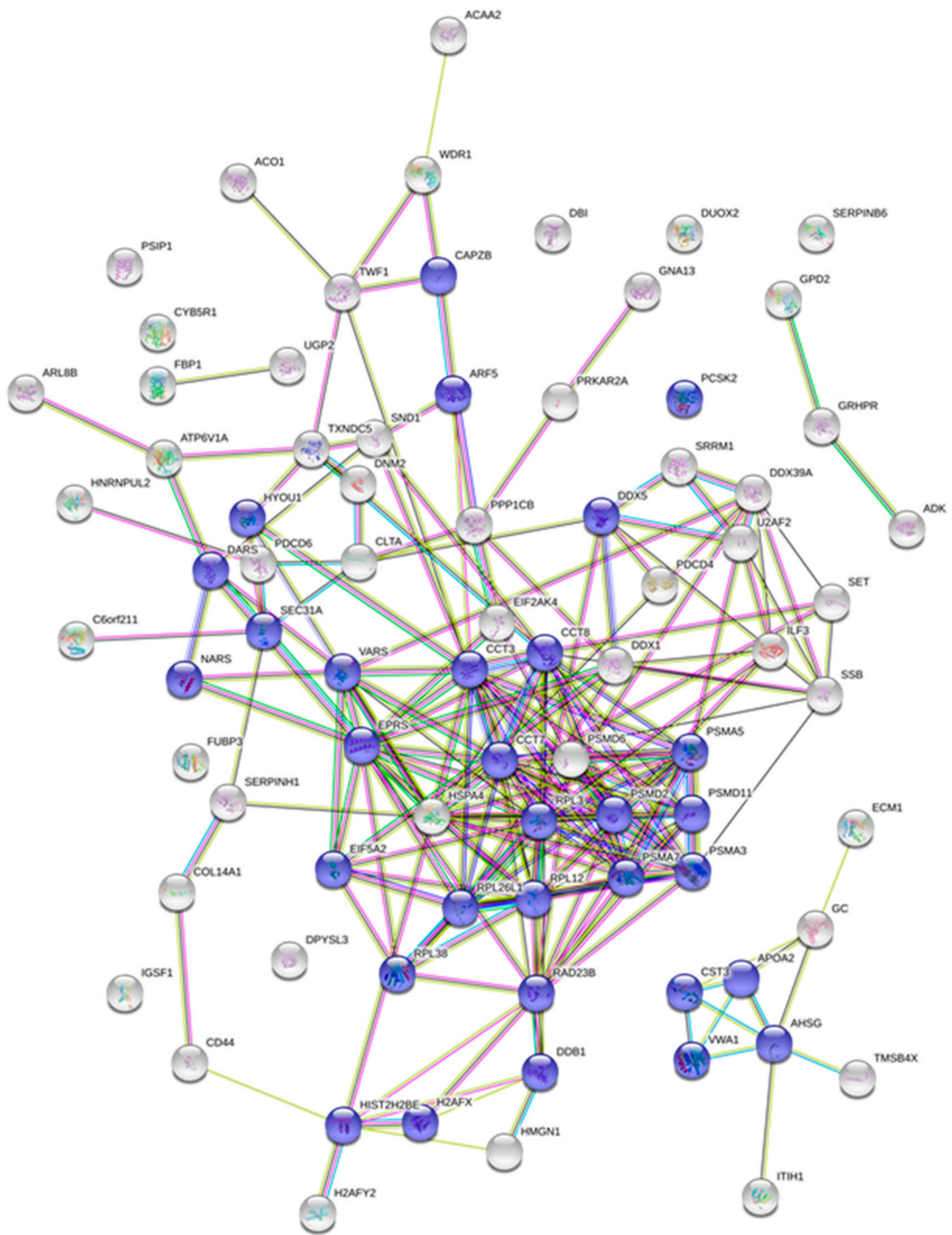


Table 1. Shared and specific molecular targets identified for the different tumor thyroid malignancies (FTA, FTC, CV-PTC and FV-PTC).

PROTEIN	UNIPROT ID	AgNPs				AuNPs				FeNPs			
		FTA (PP1)	FTC (PP2)	CV-PTC (PP3)	FV-PTC (PP4)	FTA (PP1)	FTC (PP2)	CV-PTC (PP3)	FV-PTC (PP4)	FTA (PP1)	FTC (PP2)	CV-PTC (PP3)	FV-PTC (PP4)
14-3-3 protein eta	Q04917											x	
2'-deoxynucleoside 5'-phosphate N-hydrolase 1	O43598							x					
3-hydroxybutyrate dehydrogenase type 2	Q9BUT1							x					
3-ketoacyl-CoA thiolase. mitochondrial	P42765		x										x
60S ribosomal protein L11	P62913							x					
60S ribosomal protein L3	P39023								x				x
60S acidic ribosomal protein P0-like	Q8NHW5												x
Actin. alpha cardiac muscle 1	P68032						x						
Acyl carrier protein. mitochondrial	O14561						x						
Acyl-CoA synthetase short-chain family member 3. mitochondrial	Q9H6R3			x								x	
Acyl-CoA-binding protein	P07108								x				x
Acyl-coenzyme A thioesterase	Q86TX2											x	
Acyl-coenzyme A thioesterase 13	Q9NPJ3		x					x					
Adenosine kinase	P55263								x				
Adenosylhomocysteinase 3	Q96HN2							x					
ADP/ATP translocase 1	P12235			x									
ADP/ATP translocase 4	Q9H0C2											x	
ADP-ribosylation factor 5	P84085												x
ADP-ribosylation factor-like protein 8B	Q9NVJ2								x				
Aldehyde dehydrogenase X. mitochondrial	P30837											x	
Aldo-keto reductase family 1 member C1	Q04828					x							
Alpha-2-HS-glycoprotein	P02765								x				
Antithrombin-III	P01008		x										
Apolipoprotein A-II	P02652								x				x
Asparagine--tRNA ligase. cytoplasmic	O43776								x				
Aspartate aminotransferase. cytoplasmic	P17174		x										
Aspartate--tRNA ligase. cytoplasmic	P14868								x				
ATP-dependent RNA helicase DDX39A	O00148								x				
ATP synthase mitochondrial F1 complex assembly factor 2	Q8N5M1							x					
ATP synthase subunit a	P00846											x	
ATP synthase subunit e. mitochondrial	P56385		x									x	
ATP synthase subunit g. mitochondrial	O75964											x	
ATP-dependent RNA helicase DDX1	Q92499								x				
Bifunctional glutamate/proline--tRNA ligase	P07814								x				
Calcium-binding mitochondrial carrier protein Aralar2	Q9UJS0											x	
cAMP-dependent protein kinase type II-alpha regulatory subunit	P13861								x				
Carnitine O-palmitoyltransferase 2. mitochondrial	P23786							x					
Caspase-14	P31944						x						

CD44 antigen	P16070									x				
CDGSH iron-sulfur domain-containing protein 1	Q9NZ45									x				x
Clathrin light chain A	P09496									x				
Collagen alpha-1(XIV) chain	Q05707									x				
Complement component 1 Q subcomponent-binding protein, mitochondrial	Q07021													x
Contactin-associated protein-like 4	Q9C0A0									x				
Core histone macro-H2A.2	Q9P0M6										x			
Creatine kinase B-type	P12277													x
Creatine kinase S-type, mitochondrial	P17540									x				
Cystatin-C	P01034										x			
Cytochrome b-c1 complex subunit 7	P14927													x
Cytochrome b-c1 complex subunit 8	O14949		x											x
Cytochrome b-c1 complex subunit 9	Q9UDW1									x				
Cytochrome b-c1 complex subunit Rieske, mitochondrial	P47985									x				x
Cytochrome c oxidase subunit 6B1	P14854													x
Cytochrome c oxidase subunit 7A1, mitochondrial	P24310									x				
Cytochrome c oxidase subunit NDUF4	O00483		x											
Cytoplasmic aconitate hydratase	P21399										x			
Damage-control phosphatase ARMT1	Q9H993										x			
D-beta-hydroxybutyrate dehydrogenase, mitochondrial	Q02338		x											
Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial	P30038									x				x
Delta-1-pyrroline-5-carboxylate synthase	P54886										x			
Deoxyuridine 5'-triphosphate nucleotidohydrolase, mitochondrial	P33316									x				
Dextrin	P60981										x			
DNA damage-binding protein 1	Q16531											x		
Diablo homolog, mitochondrial	Q9NR28		x							x				
Dihydropyrimidinase-related protein 3	Q14195											x		x
Dual oxidase 2	Q9NRD8											x		
Dynamin-2	P50570											x		
Electron transfer flavoprotein subunit alpha, mitochondrial	P13804		x											
eIF-2-alpha kinase GCN2	Q9P2K8											x		
Enoyl-CoA hydratase, mitochondrial	P30084													x
Estradiol 17-beta-dehydrogenase 8	Q92506											x		
Eukaryotic translation initiation factor 5A-2	Q9GZV4													x
Extracellular matrix protein 1	Q16610												x	
F-actin-capping protein subunit beta	P47756												x	
Far upstream element-binding protein 3	Q96124												x	
Fatty acid-binding protein, heart	P05413			x										x
Ferritin heavy chain	P02794			x										x
Ferritin light chain	P02792			x										x
Fibrillin-2	P35556												x	

Fructose-1,6-bisphosphatase 1	P09467								x				
Fumarate hydratase, mitochondrial	P07954		x										
Galectin-1	P09382								x				
Glutamate dehydrogenase 2, mitochondrial	P49448							x					
Glutathione S-transferase kappa 1	Q9Y2Q3								x				
Glycerol-3-phosphate dehydrogenase, mitochondrial	P43304									x			
Glycine amidinotransferase, mitochondrial	P50440			x								x	
Glyoxylate reductase/hydroxypyruvate reductase	Q9UBQ7									x			
GrpE protein homolog 1, mitochondrial	Q9HAV7								x				
Guanine nucleotide-binding protein subunit alpha-13	Q14344									x			
Guanine nucleotide-binding protein subunit beta-4	Q9HAV0							x					
Haloacid dehalogenase-like hydrolase domain-containing protein 3	Q9BSH5								x				
Heat shock 70 kDa protein 4	P34932									x			
Heat shock protein 75 kDa, mitochondrial	Q12931		x									x	
Heterogeneous nuclear ribonucleoprotein C-like 2	B2RXH8			x		x							
Heterogeneous nuclear ribonucleoprotein U-like protein 2	Q1KMD3									x			x
Hexokinase HKDC1	Q2TB90		x					x				x	
Histidine triad nucleotide-binding protein 2, mitochondrial	Q9BX68		x						x				x
Histone H1.3	P16402		x									x	
Histone H2AX	P16104												x
Histone H2B type 1-N	Q99877												x
Histone H2B type 3-B	Q8N257									x			
Hydroxymethylglutaryl-CoA lyase, mitochondrial	P35914								x				
Hypoxia up-regulated protein 1	Q9Y4L1												x
Immunoglobulin heavy constant alpha 2	P01877												x
Immunoglobulin kappa variable 2D-28	P01615							x					
Immunoglobulin kappa variable 3-11	P04433							x					
Immunoglobulin kappa variable 3-15	P01624											x	
Immunoglobulin kappa variable 3-20	P01619											x	
Immunoglobulin superfamily member 1	Q8N6C5				x					x			x
Inactive ribonuclease-like protein 10	Q5GAN6								x				
Inter-alpha-trypsin inhibitor heavy chain H1	P19827									x			
Interleukin enhancer-binding factor 3	Q12906												x
Isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial	P50213		x										
Keratin, type I cytoskeletal 15	P19012			x									
Keratin, type II cytoskeletal 1b	Q7Z794							x					
Lupus La protein	P05455									x			
Lysosome-associated membrane glycoprotein 2	P13473							x					
Medium-chain specific acyl-CoA dehydrogenase, mitochondrial	P11310			x									x

60S ribosomal protein L38	P63173									x				
Serine/arginine repetitive matrix protein 1	Q81YB3									x				
Serine/threonine-protein phosphatase PPI-beta catalytic subunit	P62140									x				
Serpin B6	P35237									x				
Serpin H1	P50454									x				
Sideroflexin-1	Q9H9B4		x				x							
Skin-specific protein 32	Q51750						x							
Splicing factor U2AF 65 kDa subunit	P26368									x				
Staphylococcal nuclease domain-containing protein 1	Q7KZF4									x				
Stomatin-like protein 2. mitochondrial	Q9UJZ1						x							
Succinate dehydrogenase [ubiquinone] flavoprotein subunit. mitochondrial	P31040												x	
Succinate dehydrogenase [ubiquinone] iron-sulfur subunit. mitochondrial	P21912							x						
Succinate--CoA ligase [GDP-forming] subunit beta. mitochondrial	Q96199												x	
Succinate-semialdehyde dehydrogenase. mitochondrial	P51649		x											
Succinyl-CoA:3-ketoacid coenzyme A transferase 1. mitochondrial	P55809		x											
Superoxide dismutase [Mn]. mitochondrial	P04179												x	
Synaptobrevin homolog YKT6	O15498												x	
T-complex protein 1 subunit eta	Q99832									x				
T-complex protein 1 subunit gamma	P49368									x				
T-complex protein 1 subunit theta	P50990									x				
Thioredoxin domain-containing protein 5	Q8NBS9									x				
Thrombospondin-1	P07996						x							
Thymosin beta-4	P62328									x				
Transcription factor A. mitochondrial	Q00059												x	
Tripeptidyl-peptidase 1	O14773											x		
Tropomyosin beta chain	P07951						x							
Tubulin beta-2B chain	Q9BVA1		x											
Twinfilin-1	Q12792									x				
UTP--glucose-1-phosphate uridylyltransferase	Q16851									x				
UV excision repair protein RAD23 homolog B	P54727									x				
Valine--tRNA ligase	P26640									x				
Vitamin D-binding protein	P02774									x				
Vitamin K-dependent protein S	P07225							x						
Voltage-dependent anion-selective channel protein 3	Q9Y277							x				x		
von Willebrand factor A domain-containing protein 1	Q6PCB0									x				
V-type proton ATPase catalytic subunit A	P38606									x				
WD repeat-containing protein 1	O75083													x

Table 2. Specific molecular targets identified for the different thyroid malignancies (FTA, FTC, CV-PTC and FV-PTC). Proteins in bold were identified in more than one subtype.

FTA <i>Follicular thyroid adenoma</i>	CV-PTC <i>Classical variant of papillary thyroid carcinoma</i>	FV-PTC <i>Follicular variant of papillary thyroid carcinoma</i>
AuNPs (<i>n</i> = 2)	AgNPs-FeNPs (<i>n</i> = 3)	AgNPs-AuNPs-FeNPs (<i>n</i> = 1)
Aldo-keto reductase family 1 member C1 (AKR1C1)	Acyl-CoA synthetase short-chain family member 3, mitochondrial (ACSS3)	Immunoglobulin superfamily member 1 (IGSF1)
Heterogeneous nuclear ribonucleoprotein C-like 2 (HNRNPCL2)	Glycine amidinotransferase, mitochondrial (GATM)	AuNPs-FeNPs (<i>n</i> = 7)
FTC <i>Follicular thyroid carcinoma</i>	Medium-chain specific acyl-CoA dehydrogenase, mitochondrial (ACADM)	Acyl-CoA-binding protein (DBI)
AgNPs-AuNPs-FeNPs (<i>n</i> = 4)	AuNPs-FeNPs (<i>n</i> = 4)	Apolipoprotein A-II (APOA2)
Fatty acid-binding protein, heart (FABP3)	CDGSH iron-sulfur domain-containing protein 1 (CISD1)	Dihydropyrimidinase-related protein 3 (DPYSL3)
Ferritin heavy chain (FTH1)	Cytochrome b-c1 complex subunit Rieske, mitochondrial (UQCRCF1)	Heterogeneous nuclear ribonucleoprotein U-like protein 2 (HNRNPUL2)
Ferritin light chain (FTL)	Histidine triad nucleotide-binding protein 2, mitochondrial (HINT2)	Neuroendocrine convertase 2 (PCSK2)
Hexokinase HKDC1 (HKDC1)	Voltage-dependent anion-selective channel protein 3 (VDAC3)	Proteasome subunit alpha type-5 (PSMA5)
AgNPs-AuNPs (<i>n</i> = 2)	AgNPs (<i>n</i> = 3)	60S ribosomal protein L3 (RPL3)
Diablo homolog, mitochondrial (DIABLO)	ADP/ATP translocase 1 (SLC25A4)	AuNPs (<i>n</i> = 73)
Sideroflexin-1 (SFXN1)	Heterogeneous nuclear ribonucleoprotein C-like 2 (HNRNPCL2)	Adenosine kinase (ADK)
AgNPs-FeNPs (<i>n</i> = 2)	Keratin, type I cytoskeletal 15 (KRT15)	ADP-ribosylation factor-like protein 8B (ARL8B)
Histone H1.3 (H1-3)	AuNPs (<i>n</i> = 24)	Alpha-2-HS-glycoprotein (AHSG)
Periostin (POSTN)	Acyl-coenzyme A thioesterase 13 (ACOT13)	Aminopeptidase B (RNPEP)
AuNPs-FeNPs (<i>n</i> = 1)	Adenosylhomocysteinase 3 (AHCYL2)	Asparagine--tRNA ligase, cytoplasmic (NARS1)
Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial (ALDH4A1)	ATP synthase mitochondrial F1 complex assembly factor 2 (ATPAF2)	Aspartate--tRNA ligase, cytoplasmic (DARS1)
AgNPs (<i>n</i> = 24)	Carnitine O-palmitoyltransferase 2, mitochondrial (CPT2)	ATP-dependent RNA helicase DDX1 (DDX1)
Acyl-coenzyme A thioesterase 13 (ACOT13)	Cytochrome b-c1 complex subunit 9 (UQCRC10)	ATP-dependent RNA helicase DDX39A (DDX39A)
Antithrombin-III (SERPINC1)	Delta-1-pyrroline-5-carboxylate synthase (ALDH18A1)	Bifunctional glutamate/proline--tRNA ligase (EPRS1)
Aspartate aminotransferase, cytoplasmic (GOT1)	2'-deoxynucleoside 5'-phosphate N-hydrolase 1 (DNPH1)	cAMP-dependent protein kinase type II-alpha regulatory subunit (PRKAR2A)
ATP synthase subunit e, mitochondrial (ATP5ME)	Destrin (DSTN)	CD44 antigen (CD44)
Cytochrome b-c1 complex subunit 8 (UQCRCQ)	Estradiol 17-beta-dehydrogenase 8 (HSD17B8)	Clathrin light chain A (CLTA)
Cytochrome c oxidase subunit NDUFA4 (NDUFA4)	Fibrillin-2 (FBN2)	Collagen alpha-1(XIV) chain (COL14A1)
D-beta-hydroxybutyrate dehydrogenase, mitochondrial (BDH1)	Galectin-1 (LGALS1)	Core histone macro-H2A.2 (MACROH2A2)
Electron transfer flavoprotein subunit alpha, mitochondrial (ETFa)	Glutathione S-transferase kappa 1 (GSTK1)	Cystatin-C (CST3)
Fumarate hydratase, mitochondrial (FH)	GrpE protein homolog 1, mitochondrial (GRPEL1)	Cytoplasmic aconitate hydratase (ACO1)
Heat shock protein 75 kDa, mitochondrial (TRAP1)	Haloacid dehalogenase-like hydrolase domain-containing protein 3 (HDHD3)	Damage-control phosphatase ARMT1 (ARMT1)
Histidine triad nucleotide-binding protein 2, mitochondrial (HINT2)	3-hydroxybutyrate dehydrogenase type 2 (BDH2)	DNA damage-binding protein 1 (DDB1)
Isocitrate dehydrogenase [NAD] subunit alpha, mitochondrial (IDH3A)	Hydroxymethylglutaryl-CoA lyase, mitochondrial (HMGCL)	Dual oxidase 2 (DUOX2)
3-ketoacyl-CoA thiolase, mitochondrial (ACAA2)	Inactive ribonuclease-like protein 10 (RNASE10)	Dynamin-2 (DNM2)
Mitochondrial carrier homolog 2 (MTCH2)	NAD kinase 2, mitochondrial (NADK2)	EF-hand domain-containing protein D2 (EFHD2)
Mitochondrial 2-oxoglutarate/malate carrier protein (SLC25A11)	Plasminogen receptor (KT) (PLGRKT)	eIF-2-alpha kinase GCN2 (EIF2AK4)
Myosin light chain 6B (MYL6B)	Protein FMC1 homolog (FMC1)	Extracellular matrix protein 1 (ECM1)
NPC intracellular cholesterol transporter 2 (NPC2)	Protein NipSnap homolog 3A (NIPSNAP3A)	F-actin-capping protein subunit beta (CAPZB)
Peptidyl-prolyl cis-trans isomerase F, mitochondrial (PPIF)	60S ribosomal protein L11 (RPL11)	Far upstream element-binding protein 3 (FUBP3)
Propionyl-CoA carboxylase alpha chain, mitochondrial (PCCA)	Succinate dehydrogenase [ubiquinone] iron-sulfur subunit, mitochondrial (SDHB)	Flotillin-1 (FLOT1)
Protein ABHD11 (ABHD11)	Vitamin K-dependent protein S (PROS1)	Fructose-1,6-bisphosphatase 1 (FBP1)
		Glycerol-3-phosphate dehydrogenase, mitochondrial (GPD2)
		Glyoxylate reductase/hydroxypyruvate reductase (GRHPR)
		Guanine nucleotide-binding protein subunit alpha-13 (GNA13)
		Heat shock 70 kDa protein 4 (HSPA4)

Pyruvate kinase PKLR (PKLR)	<i>FeNPs</i> (n = 29)	Histone H2B type 3-B (H2BU1)
Succinate-semialdehyde dehydrogenase, mitochondrial (ALDH5A1)	Acyl-coenzyme A thioesterase 1 (ACOT1)	Inter-alpha-trypsin inhibitor heavy chain H1 (ITI1H1) Leucine-rich repeat-containing protein 47 (LRRRC47)
Succinyl-CoA:3-ketoacid coenzyme A transferase 1, mitochondrial (OXCT1)	ADP/ATP translocase 4 (SLC25A31)	Lupus La protein (SSB)
Tubulin beta-2B chain (TUBB2B)	Aldehyde dehydrogenase X, mitochondrial (ALDH1B1)	NADH-cytochrome b5 reductase 1 (CYB5R1) N(G),N(G)-dimethylarginine dimethylaminohydrolase 1 (DDAH1)
<i>AuNPs</i> (n = 21)	ATP synthase subunit a (MT-ATP6)	Non-histone chromosomal protein HMG-14 (HMGN1)
Actin, alpha cardiac muscle 1 (ACTC1)	ATP synthase subunit e, mitochondrial (ATP5ME)	PC4 and SFRS1-interacting protein (PSIP1) Plastin-1 (PLS1)
Acyl carrier protein, mitochondrial (NDUFAB1)	ATP synthase subunit g, mitochondrial (ATP5MG)	Probable ATP-dependent RNA helicase DDX5 (DDX5)
Caspase-14 (CASP14)	Calcium-binding mitochondrial carrier protein Aralar2 (SLC25A13)	Programmed cell death protein 4 (PDCD4)
Contactin-associated protein-like 4 (CNTNAP4)	Complement component 1 Q subcomponent-binding protein, mitochondrial (C1QBP)	Programmed cell death protein 6 (PDCD6)
Creatine kinase S-type, mitochondrial (CKMT2)	Creatine kinase B-type (CKB)	Proteasome subunit alpha type-3 (PSMA3) Proteasome subunit alpha type-6 (PSMA6)
Cytochrome c oxidase subunit 7A1, mitochondrial (COX7A1)	Cytochrome b-c1 complex subunit 7 (UQCRB)	Proteasome subunit alpha type-7 (PSMA7)
Deoxyuridine 5'-triphosphate nucleotidohydrolase, mitochondrial (DUT)	Cytochrome b-c1 complex subunit 8 (UQCRQ)	Protein transport protein Sec31A (SEC31A)
Glutamate dehydrogenase 2, mitochondrial (GLUD2)	Cytochrome c oxidase subunit 6B1 (COX6B1)	26S proteasome non-ATPase regulatory subunit 2 (PSMD2)
Guanine nucleotide-binding protein subunit beta-4 (GNB4)	Enoyl-CoA hydratase, mitochondrial (ECHS1)	26S proteasome non-ATPase regulatory subunit 6 (PSMD6)
Immunoglobulin kappa variable 2D-28 (IGKV2D-28)	Heat shock protein 75 kDa, mitochondrial (TRAP1)	26S proteasome non-ATPase regulatory subunit 11 (PSMD11) 26S proteasome non-ATPase regulatory subunit 12 (PSMD12) Rho GDP-dissociation inhibitor 1 (ARHGDI1A)
Immunoglobulin kappa variable 3-11 (IGKV3-11)	Histone H2B type 1-N (H2BC15)	60S ribosomal protein L26-like 1 (RPL26L1)
Keratin, type II cytoskeletal 1b (KRT77)	Immunoglobulin heavy constant alpha 2 (IGHA2)	60S ribosomal protein L38 (RPL38)
Lysosome-associated membrane glycoprotein 2 (LAMP2)	Methylmalonate-semialdehyde dehydrogenase [acylating], mitochondrial (ALDH6A1)	Serine/arginine repetitive matrix protein 1 (SRRM1)
Monocyte differentiation antigen CD14 (CD14)	MICOS complex subunit MIC60 (IMMT)	Serine/threonine-protein phosphatase PP1-beta catalytic subunit (PPP1CB)
NADPH:adrenodoxin oxidoreductase, mitochondrial (FDXR)	Mycophenolic acid acyl-glucuronide esterase, mitochondrial (ABHD10)	Serpin B6 (SERPINB6)
Propionyl-CoA carboxylase beta chain, mitochondrial (PCCB)	Peptidyl-prolyl cis-trans isomerase F, mitochondrial (PPIF)	Serpin H1 (SERPINH1)
Protein FAM162A (FAM162A)	Phosphoenolpyruvate carboxykinase [GTP], mitochondrial (PCK2)	Splicing factor U2AF 65 kDa subunit (U2AF2)
Skin-specific protein 32 (XP32)	Protein ABHD11 (ABHD11)	Staphylococcal nuclease domain-containing protein 1 (SND1)
Stomatin-like protein 2, mitochondrial (STOML2)	14-3-3 protein eta (YWHAH)	T-complex protein 1 subunit eta (Q99832)
Thrombospondin-1 (THBS1)	Pyruvate dehydrogenase E1 component subunit beta, mitochondrial (PDHB)	T-complex protein 1 subunit gamma (CCT3)
Tropomyosin beta chain (TPM2)	Succinate--CoA ligase [GDP-forming] subunit beta, mitochondrial (SUCLG2)	T-complex protein 1 subunit theta (CCT8)
<i>FeNPs</i> (n = 3)	Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial (SDHA)	Thioredoxin domain-containing protein 5 (TXNDC5)
Immunoglobulin kappa variable 3-15 (IGKV3-15)	Superoxide dismutase [Mn], mitochondrial (SOD2)	Thymosin beta-4 (TMSB4X) Tryptophan--tRNA ligase, cytoplasmic (WARS1)
Immunoglobulin kappa variable 3-20 (IGKV3-20)	Synaptobrevin homolog YKT6 (YKT6)	Twinfilin-1 (TWF1)
Tripeptidyl-peptidase 1 (TPP1)	Transcription factor A, mitochondrial (TFAM)	UTP--glucose-1-phosphate uridylyltransferase (UGP2) UV excision repair protein RAD23 homolog B (RAD23B) Valine--tRNA ligase (VARS1) Vitamin D-binding protein (GC) von Willebrand factor A domain-containing protein 1 (VWA1) V-type proton ATPase catalytic subunit A (ATP6V1A)

<i>FeNPs</i> ($n = 10$)
ADP-ribosylation factor 5 (ARF5)
60S acidic ribosomal protein P0-like (RPLP0P6)
Eukaryotic translation initiation factor 5A-2 (EIF5A2)
Histone H2AX (H2AX)
Hypoxia up-regulated protein 1 (HYOU1)
Interleukin enhancer-binding factor 3 (ILF3)
3-ketoacyl-CoA thiolase, mitochondrial (ACAA2)
Protein SET (SET)
60S ribosomal protein L12 (RPL12)
WD repeat-containing protein 1 (WDR1)