Supplementary Information

Intratumoral Generation of Photothermal Gold Nanoparticles through a Vectorized Biomineralization of Ionic Gold

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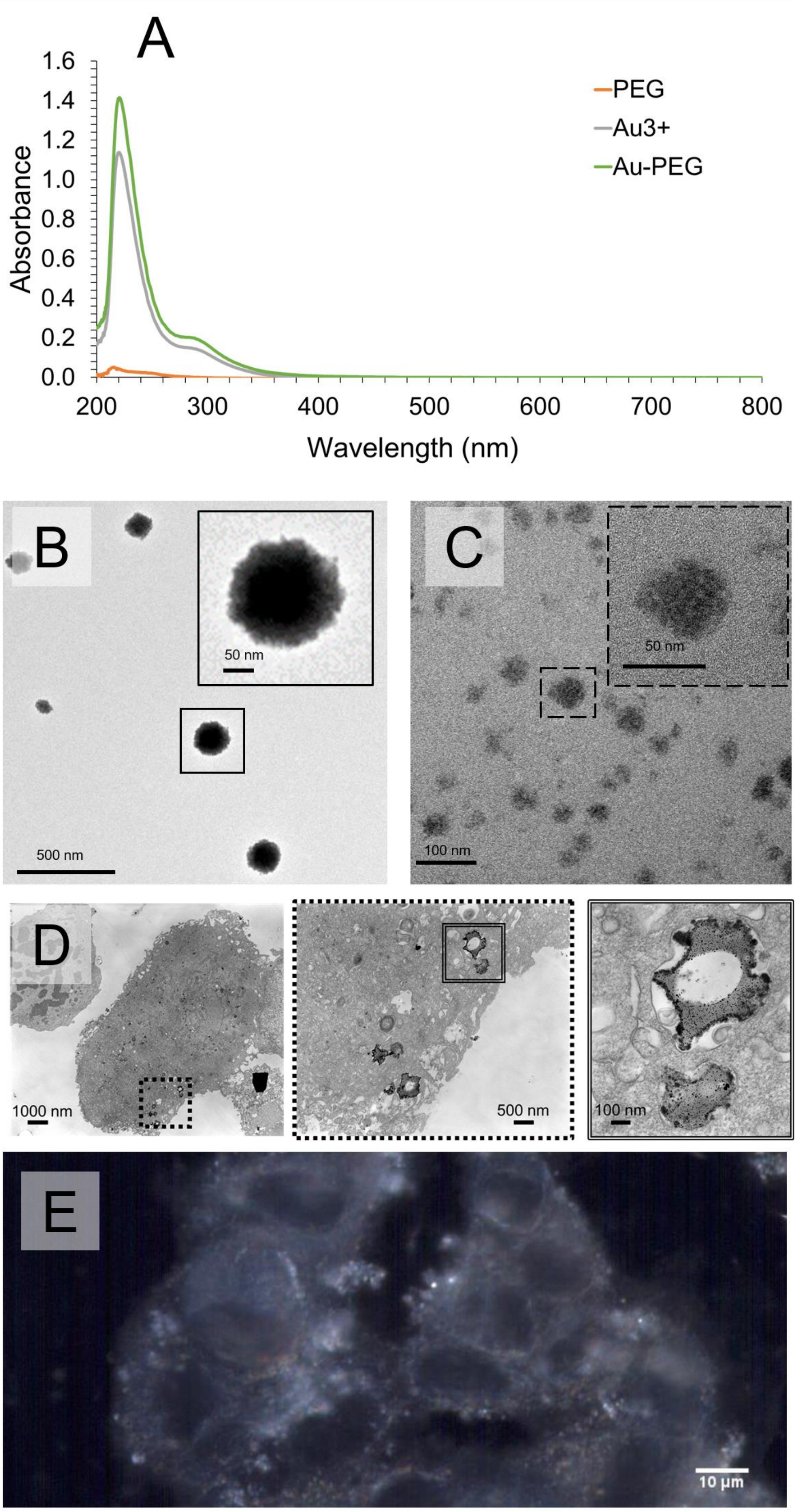
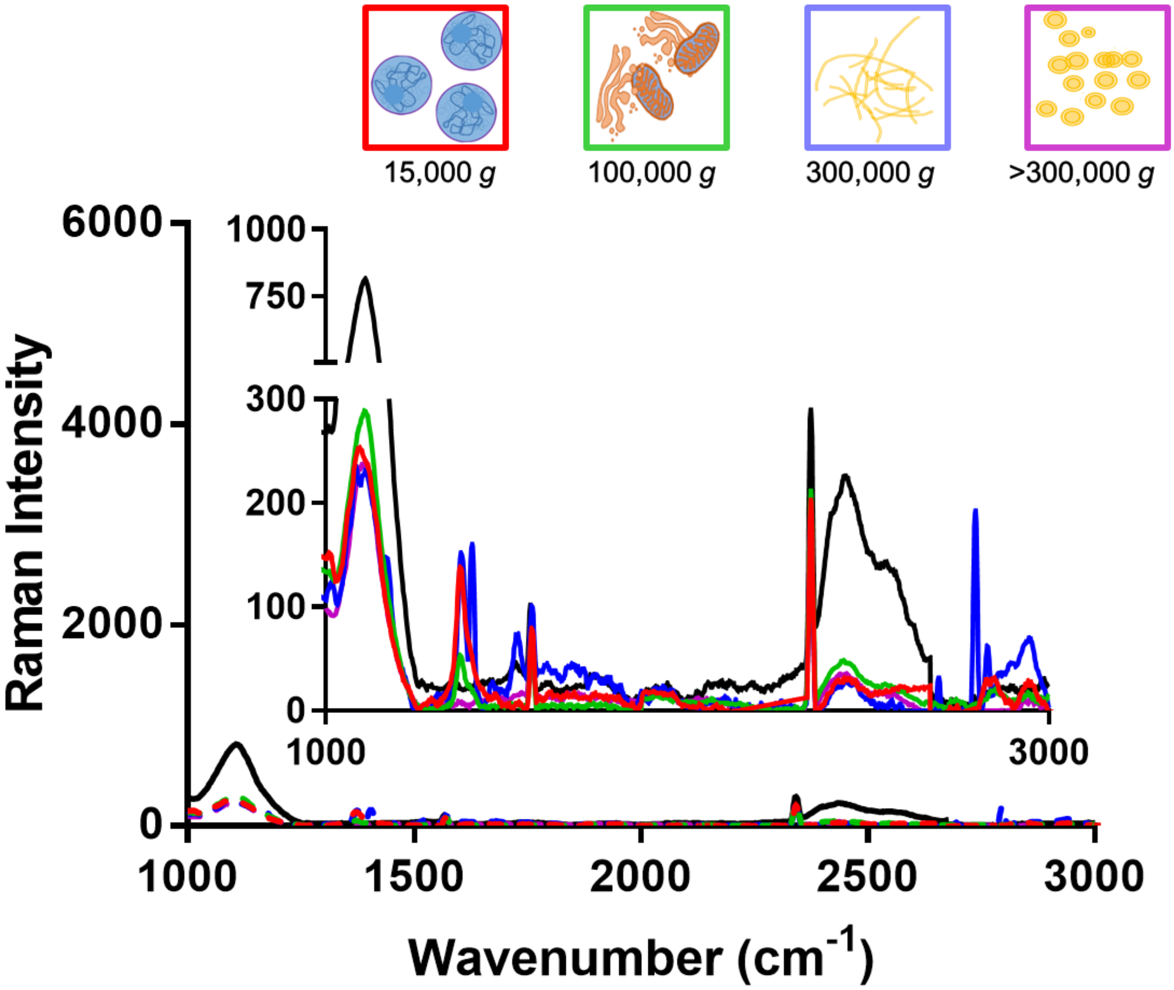
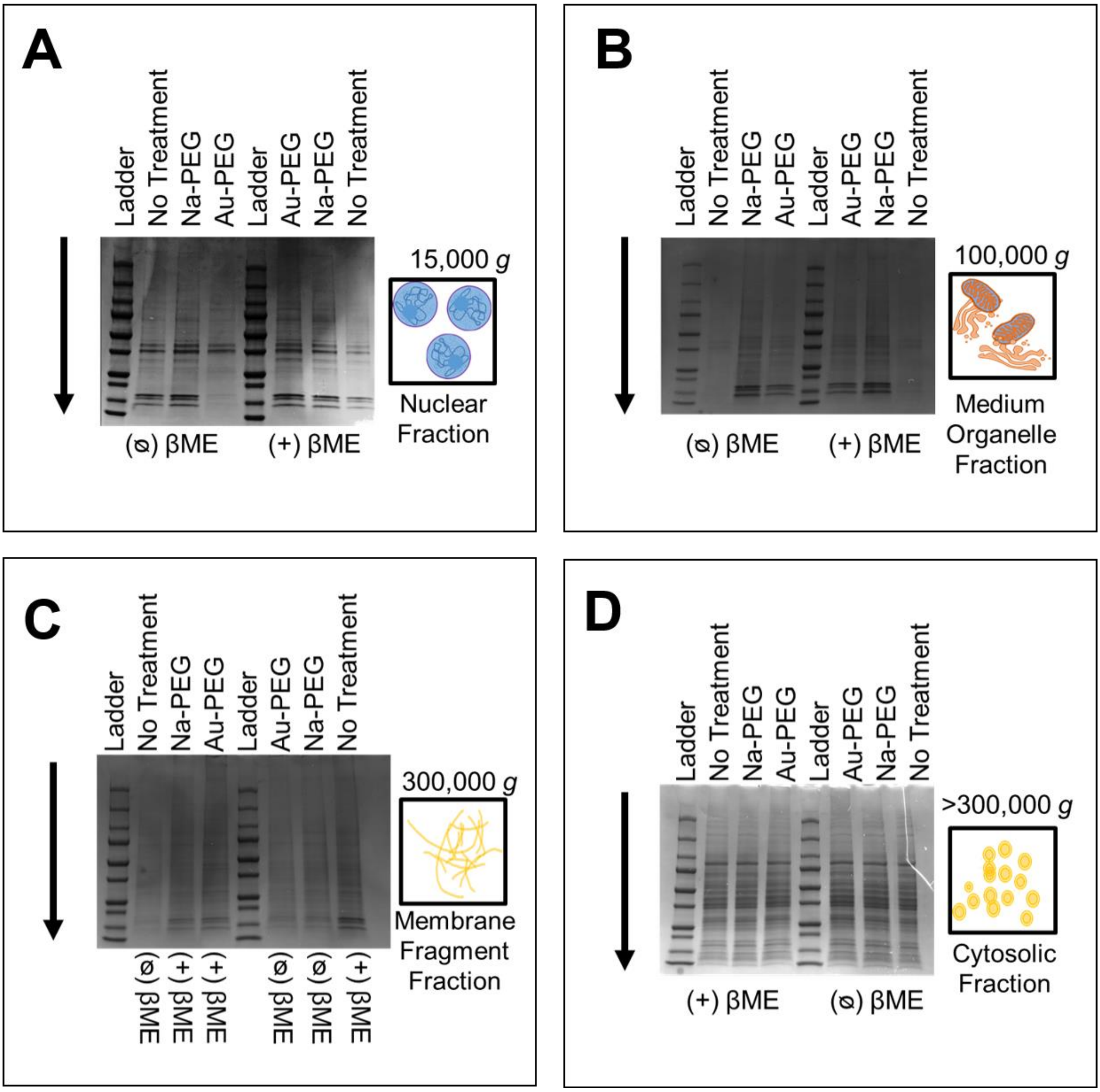


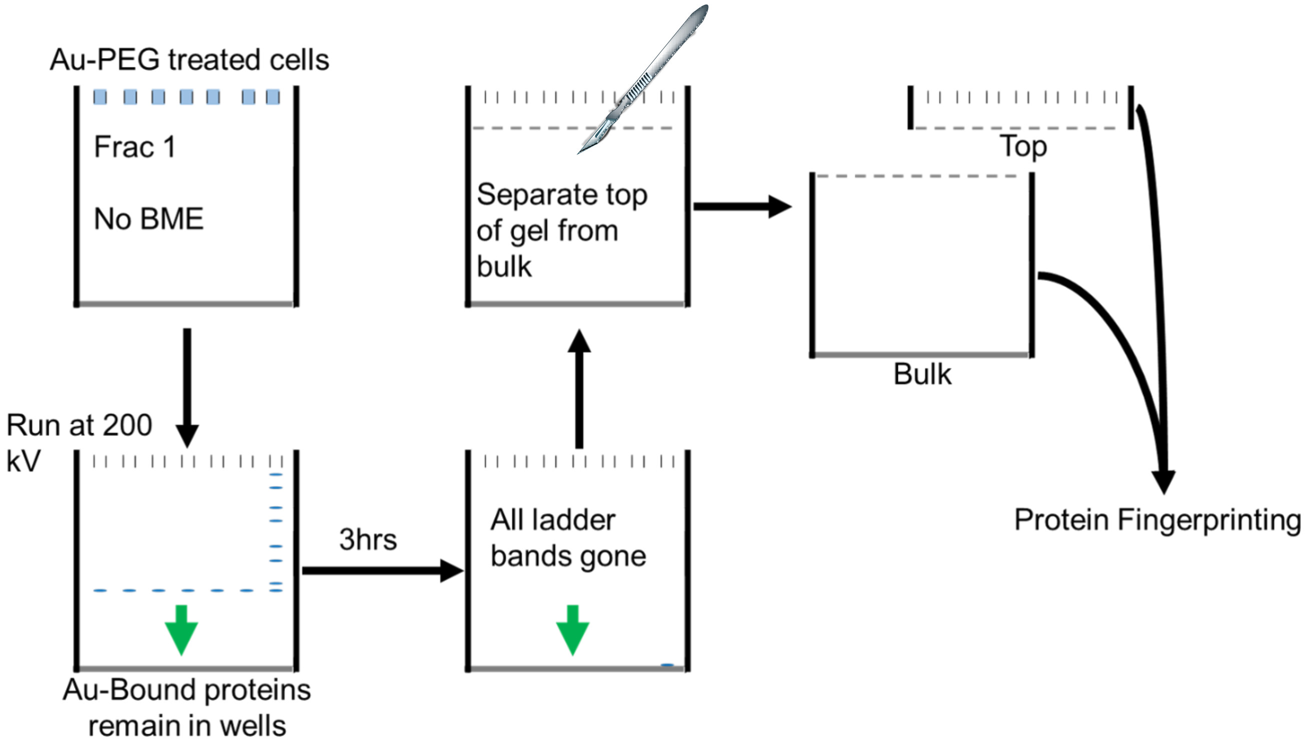
Supplementary Figure 1. Characterization of ionic Au-PEG cluster: (A) UV-Vis absorbance spectra of ionic Au-PEG clusters (200-800 nm) as well as it's individual components at identical concentrations. TEM images from the extracted solution of ionic Au-PEG treatments to cell culture plates with a magnification of Au-PEG cluster (B), and fresh cell culture media incubated with Au-PEG clusters (C). Additional TEM images of Au-PEG treated MCF-7 cells at various magnifications (D). Enhanced hyperspectral darkfield image of untreated MCF-7 cells used for negative filtering for Figure 2A and 2B (E).



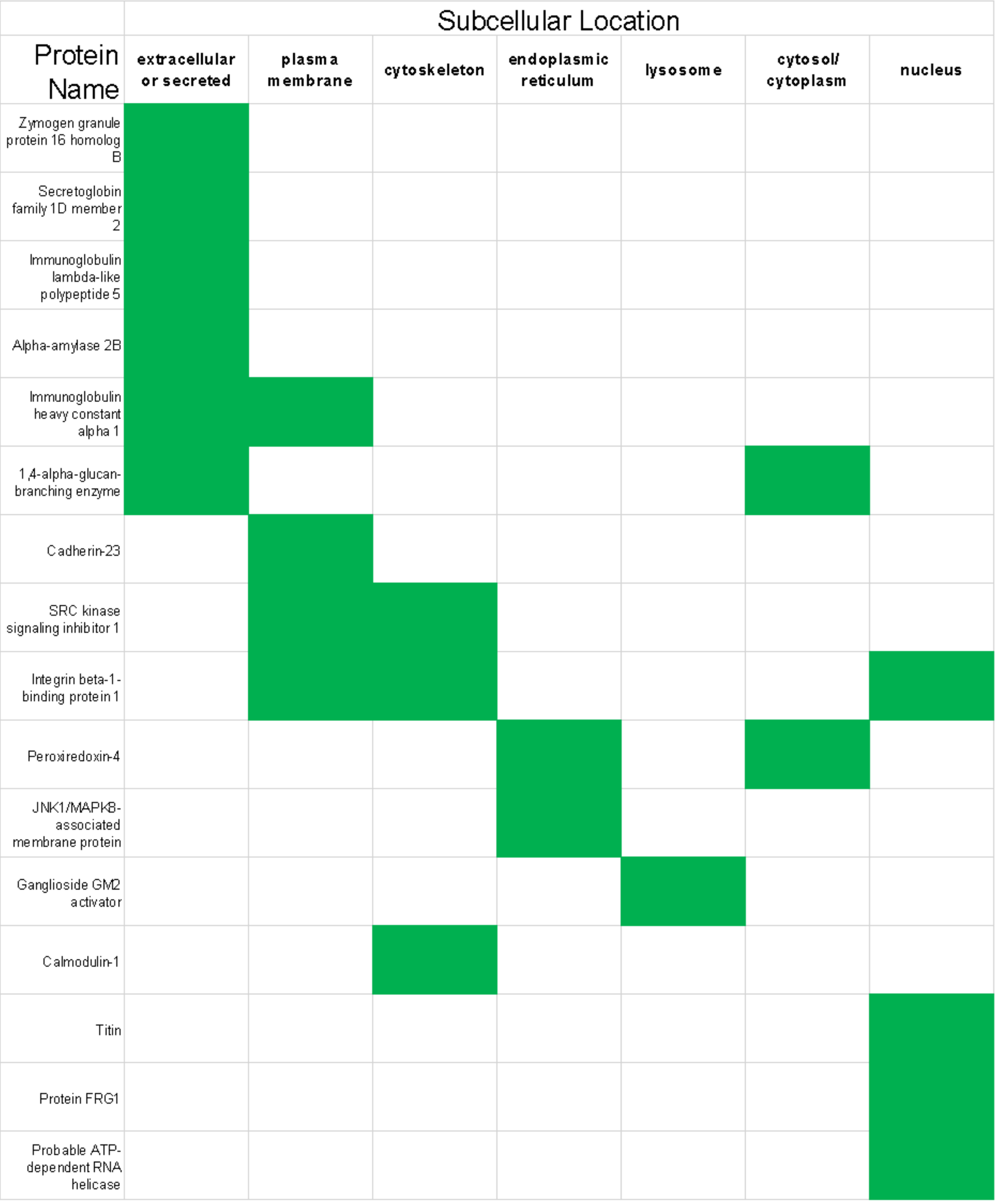
Supplementary Figure 2. Raman spectra of cellular fractions (all from MCF-7 cells): Nucleus and large organelles, 15,000 *g* (Red); mitochondria, lysosomes, and other medium sized organelles, 100,000 *g* (Green); membrane fragments, 300,000 *g* (Blue); and highly soluble/cytosolic molecules (Violet), >300,000 *g*; and the glass slide without cell fractions (Black).



Supplementary Figure 3. Confirmation of intracellular reduction by SDS-PAGE: SDS-PAGE stained with Coomassie Blue of cellular fractions including (A) nuclear, 15,000 *g*; (B) medium organelle, 100,000 *g*; (C) membrane fragments, 300,000 *g*; and (D) cytosolic, >300,000 *g* regions of MCF-7 cells untreated, treated with Na-PEG, or Au-PEG with either standard SDS-PAGE conditions [(+) βME], or without β-mercaptoethanol [(⊘) βME]. Arrows indicate direction of protein migration due to electrophoresis.

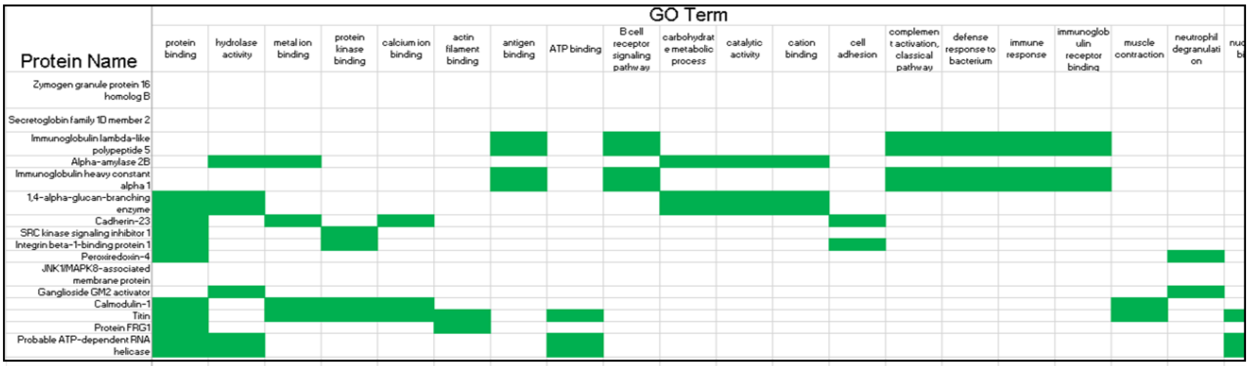


Supplementary Figure 4. Schematic for separation of Au bound proteins from the non-bounded ones: The process describing the separation of Au-bound proteins from non-bound ones through gel electrophoresis, followed by separation of portions of the gel for LC-MS analysis.

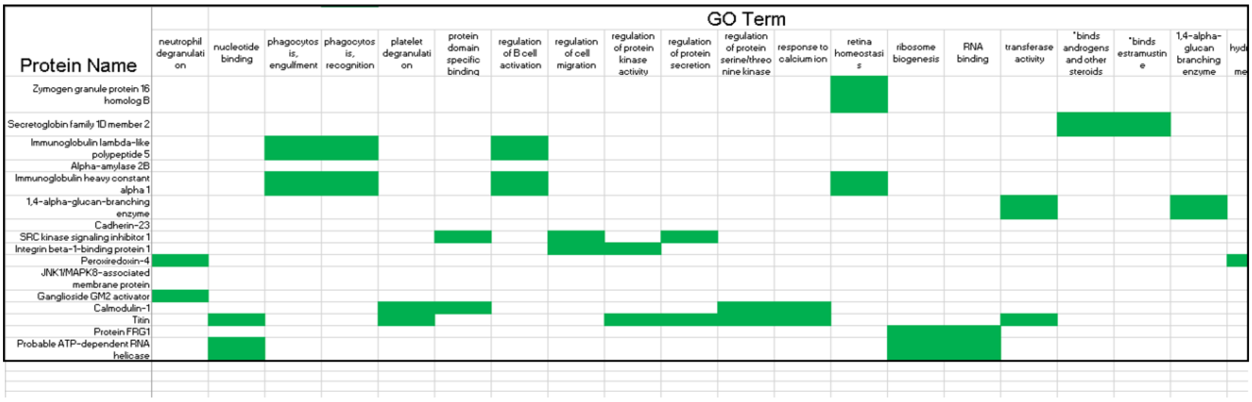


Protein Name	Subcellular Location						
	extracellular or secreted	plasma membrane	cytoskeleton	endoplasmic reticulum	lysosome	cytosol/ cytoplasm	nucleus
Zymogen granule protein 16 homolog B	🟩						
Secretoglobin family 1D member 2	🟩						
Immunoglobulin lambda-like polypeptide 5	🟩						
Alpha-amylase 2B	🟩						
Immunoglobulin heavy constant alpha 1	🟩	🟩					
1,4-alpha-glucan-branching enzyme	🟩					🟩	
Cadherin-23		🟩					
SRC kinase signaling inhibitor 1		🟩	🟩				
Integrin beta-1-binding protein 1		🟩	🟩				🟩
Peroxiredoxin-4				🟩		🟩	
JNK1/MAPK8-associated membrane protein				🟩			
Ganglioside GM2 activator					🟩		
Calmodulin-1			🟩				
Titin							🟩
Protein FRG1							🟩
Probable ATP-dependent RNA helicase							🟩

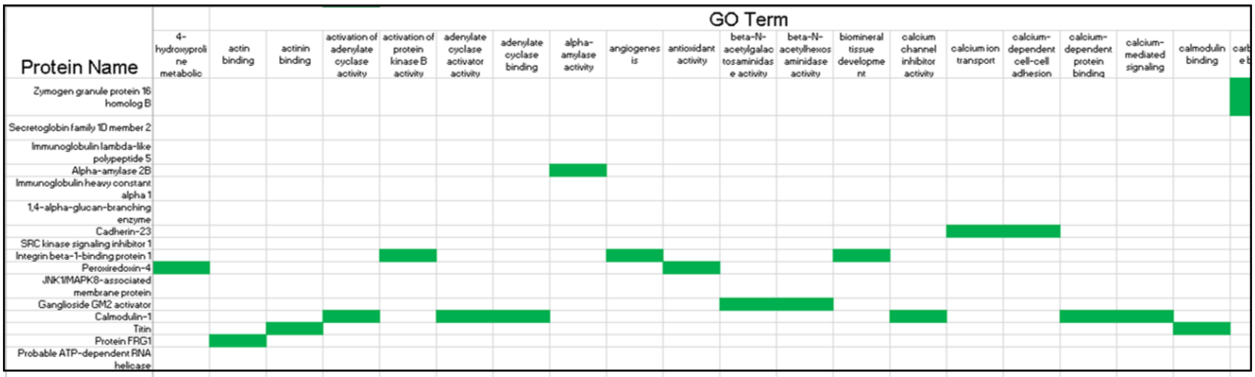
Supplementary Table 1. Proteins identified from the LC-MS analysis and the subcellular regions in which they are located, as annotated on UniProt.org through COMPARTMENTS.[1]



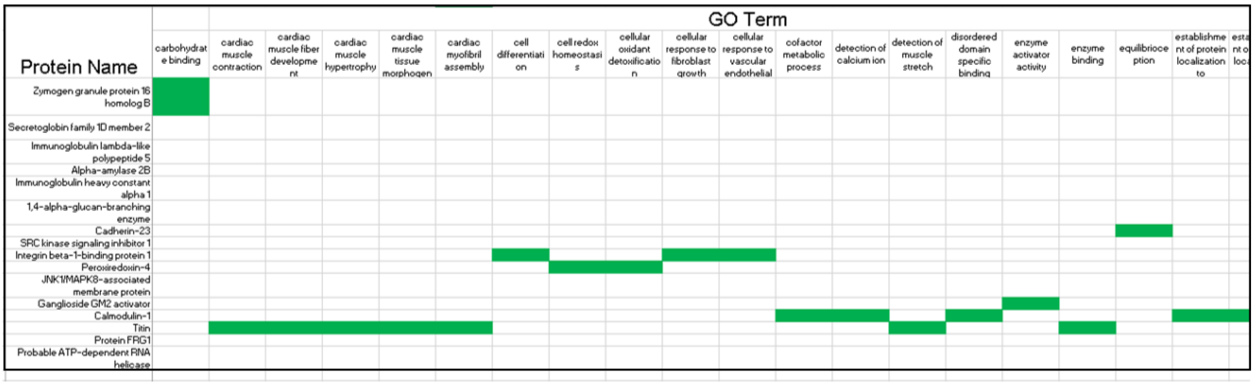
Protein Name	GO Term																			
	protein binding	hydrolase activity	metal ion binding	protein kinase binding	calcium ion binding	actin filament binding	antigen binding	ATP binding	B cell receptor signaling pathway	carbohydrate metabolic process	catalytic activity	cation binding	cell adhesion	complement activation, classical pathway	defense response to bacterium	immune response	immunoglobulin receptor binding	muscle contraction	neutrophil degranulation	nuc bi
Zymogen granule protein 16 homolog B																				
Secretoglobin family 1D member 2																				
Immunoglobulin lambda-like polypeptide 5							🟩		🟩					🟩	🟩	🟩	🟩			
Alpha-amylase 2B		🟩	🟩							🟩	🟩	🟩								
Immunoglobulin heavy constant alpha 1							🟩		🟩					🟩	🟩	🟩	🟩			
1,4-alpha-glucan-branching enzyme	🟩	🟩								🟩	🟩	🟩								
Cadherin-23	🟩		🟩		🟩								🟩							
SRC kinase signaling inhibitor 1	🟩			🟩																
Integrin beta-1-binding protein 1	🟩			🟩									🟩							
Peroxiredoxin-4	🟩																		🟩	
JNK1/MAPK8-associated membrane protein																				
Ganglioside GM2 activator		🟩																	🟩	
Calmodulin-1	🟩		🟩	🟩	🟩													🟩		
Titin	🟩		🟩	🟩	🟩	🟩		🟩										🟩		🟩
Protein FRG1	🟩					🟩														
Probable ATP-dependent RNA helicase	🟩	🟩						🟩												🟩



Protein Name	GO Term																			
	neutrophil degranulation	nucleotide binding	phagocytosis, engulfment	phagocytosis, recognition	platelet degranulation	protein domain specific binding	regulation of B cell activation	regulation of cell migration	regulation of protein kinase activity	regulation of protein secretion	regulation of protein serine/threonine kinase	response to calcium ion	retina homeostasis	ribosome biogenesis	RNA binding	transferase activity	*binds androgens and other steroids	*binds estramustine	1,4-alpha-glucan branching enzyme	hyd me
Zymogen granule protein 16 homolog B													🟩							
Secretoglobin family 1D member 2																	🟩	🟩		
Immunoglobulin lambda-like polypeptide 5			🟩	🟩			🟩													
Alpha-amylase 2B																				
Immunoglobulin heavy constant alpha 1			🟩	🟩			🟩						🟩							
1,4-alpha-glucan-branching enzyme																🟩			🟩	
Cadherin-23																				
SRC kinase signaling inhibitor 1						🟩		🟩		🟩										
Integrin beta-1-binding protein 1								🟩	🟩											
Peroxiredoxin-4	🟩																			🟩
JNK1/MAPK8-associated membrane protein																				
Ganglioside GM2 activator	🟩																			
Calmodulin-1					🟩	🟩					🟩	🟩								
Titin		🟩			🟩				🟩	🟩	🟩	🟩				🟩				
Protein FRG1														🟩	🟩					
Probable ATP-dependent RNA helicase		🟩												🟩	🟩					

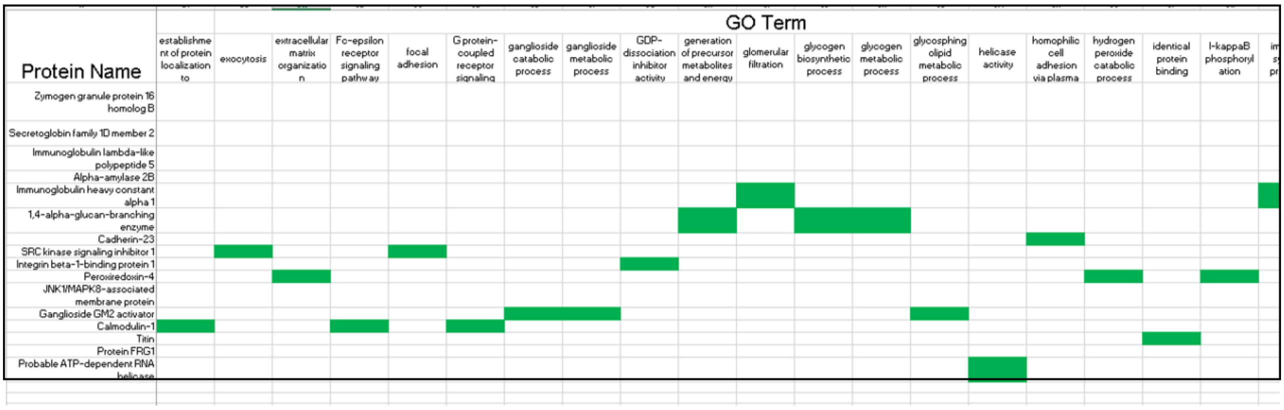


Protein Name	GO Term																			
	4-hydroxyproline metabolic	actin binding	actinin binding	activation of adenylate cyclase activity	activation of protein kinase B activity	adenylate cyclase activator activity	adenylate cyclase binding	alpha-amylase activity	angiogenesis	antioxidant activity	beta-N-acetylgalactosaminidase activity	beta-N-acetylhexosaminidase activity	biomineral tissue development	calcium channel inhibitor activity	calcium ion transport	calcium-dependent cell-cell adhesion	calcium-dependent protein binding	calcium-mediated signaling	calmodulin binding	carb e b
Zymogen granule protein 16 homolog B																				🟩
Secretoglobin family 1D member 2																				
Immunoglobulin lambda-like polypeptide 5																				
Alpha-amylase 2B								🟩												
Immunoglobulin heavy constant alpha 1																				
1,4-alpha-glucan-branching enzyme																				
Cadherin-23															🟩	🟩				
SRC kinase signaling inhibitor 1																				
Integrin beta-1-binding protein 1					🟩				🟩				🟩							
Peroxiredoxin-4	🟩									🟩										
JNK1/MAPK8-associated membrane protein																				
Ganglioside GM2 activator											🟩	🟩								
Calmodulin-1				🟩		🟩	🟩							🟩			🟩	🟩		
Titin			🟩																🟩	
Protein FRG1		🟩																		
Probable ATP-dependent RNA helicase																				



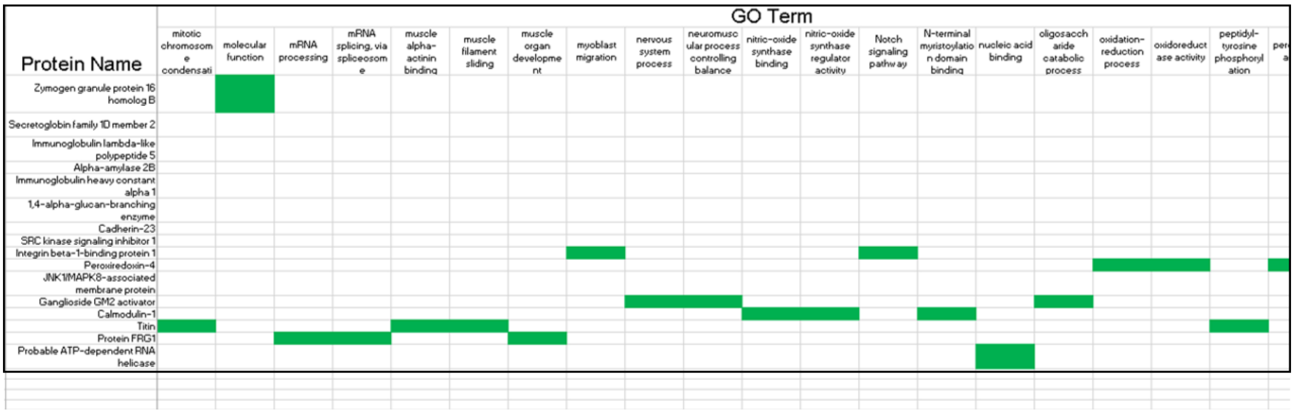
Protein Name	GO Term																			
	carbohydrate binding	cardiac muscle contraction	cardiac muscle fiber development	cardiac muscle hypertrophy	cardiac muscle tissue morphogen	cardiac myofibril assembly	cell differentiation	cell redox homeostasis	cellular oxidant detoxification	cellular response to fibroblast growth	cellular response to vascular endothelial	cofactor metabolic process	detection of calcium ion	detection of muscle stretch	disordered domain specific binding	enzyme activator activity	enzyme binding	equilibrioception	establishment of protein localization to	esta nt o loca
Zymogen granule protein 16 homolog B	🟩																			
Secretoglobin family 1D member 2																				
Immunoglobulin lambda-like polypeptide 5																				
Alpha-amylase 2B																				
Immunoglobulin heavy constant alpha 1																				
1,4-alpha-glucan-branching enzyme																				
Cadherin-23																		🟩		
SRC kinase signaling inhibitor 1																				
Integrin beta-1-binding protein 1							🟩			🟩	🟩									
Peroxiredoxin-4								🟩	🟩											
JNK1/MAPK8-associated membrane protein																				
Ganglioside GM2 activator																🟩				
Calmodulin-1												🟩	🟩		🟩				🟩	🟩
Titin		🟩	🟩	🟩	🟩	🟩								🟩			🟩			
Protein FRG1																				
Probable ATP-dependent RNA helicase																				

Supplementary Table 2. Proteins identified from the LC-MS analysis and the molecular processes in which they are involved, as annotated on UniProt.org through phylogenetic-based propagation of functional gene ontology (GO) annotations.[2]

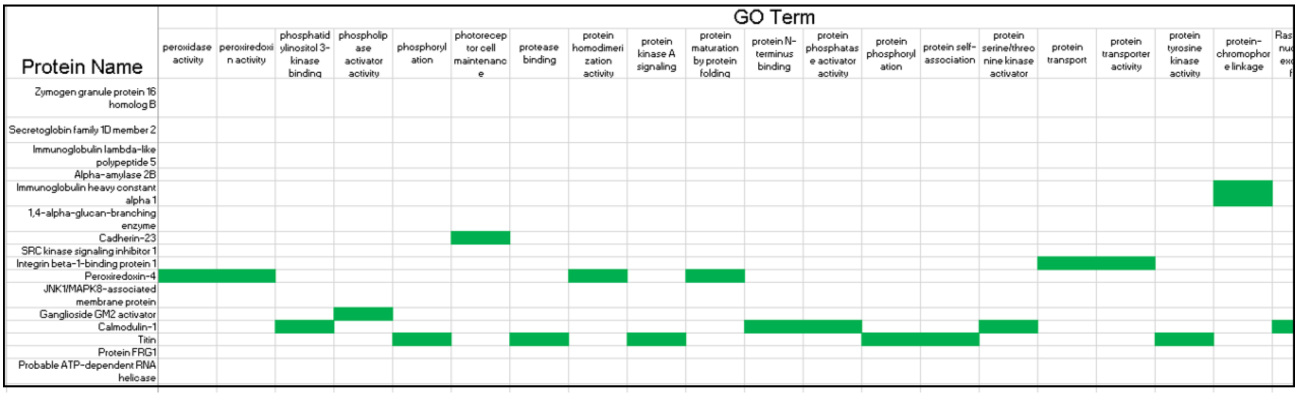


Protein Name	GO Term																			
	establishment of protein localization to	exocytosis	extracellular matrix organization	Fc-epsilon receptor signaling pathway	focal adhesion	G protein-coupled receptor signaling	ganglioside catabolic process	ganglioside metabolic process	GDP-dissociation inhibitor activity	generation of precursor metabolites and energy	glomerular filtration	glycogen biosynthetic process	glycogen metabolic process	glycosphingolipid metabolic process	helicase activity	homophilic cell adhesion via plasma	hydrogen peroxide catabolic process	identical protein binding	I-kappaB phosphorylation	im s pr
Zymogen granule protein 16 homolog B																				
Secretoglobin family 1D member 2																				
Immunoglobulin lambda-like polypeptide 5																				
Alpha-amylase 2B																				
Immunoglobulin heavy constant alpha 1											🟩									🟩
1,4-alpha-glucan-branching enzyme										🟩		🟩	🟩							
Cadherin-23																🟩				
SRC kinase signaling inhibitor 1		🟩			🟩															
Integrin beta-1-binding protein 1									🟩											
Peroxiredoxin-4			🟩														🟩		🟩	
JNK1/MAPK8-associated membrane protein																				
Ganglioside GM2 activator							🟩	🟩						🟩						
Calmodulin-1	🟩			🟩		🟩														
Titin																		🟩		
Protein FRG1																				
Probable ATP-dependent RNA helicase															🟩					

Protein Name	GO Term																			
	immune system process	inner ear receptor cell stereocilium	inositol phosphate metabolic process	inositol-1,4,5-trisphosphate 3-kinase	integrin activation	integrin binding	integrin-mediated signaling pathway	intracellular signal transduction	ion channel binding	kinase activity	learning or memory	leukocyte migration	lipid metabolic process	lipid storage	lipid transporter activity	locomotory behavior	male gonad development	MAPK cascade	metabolic process	m chr cor
Zymogen granule protein 16 homolog B																				
Secretoglobin family 1D member 2																				
Immunoglobulin lambda-like polypeptide 5																				
Alpha-amylase 2B																			🟩	
Immunoglobulin heavy constant alpha 1	🟩											🟩								
1,4-alpha-glucan-branching enzyme																				
Cadherin-23		🟩														🟩				
SRC kinase signaling inhibitor 1																				
Integrin beta-1-binding protein 1					🟩	🟩	🟩	🟩												
Peroxiredoxin-4																	🟩			
JNK1/MAPK8-associated membrane protein																				
Ganglioside GM2 activator											🟩		🟩	🟩	🟩					
Calmodulin-1			🟩	🟩					🟩									🟩		
Titin										🟩										🟩
Protein FRG1																				
Probable ATP-dependent RNA helicase																				

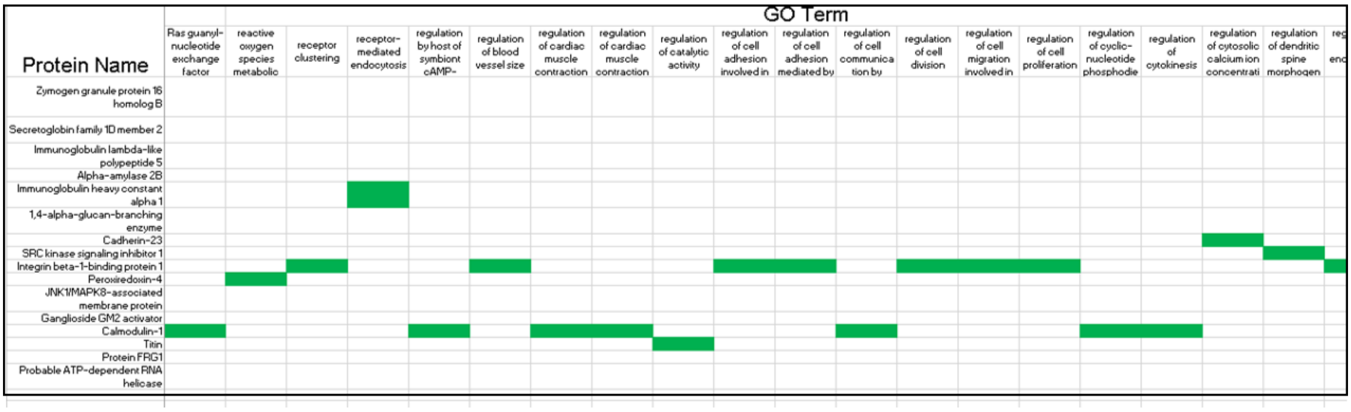


Protein Name	GO Term																			
	mitotic chromosome condensati	molecular function	mRNA processing	mRNA splicing, via spliceosome	muscle alpha-actinin binding	muscle filament sliding	muscle organ development	myoblast migration	nervous system process	neuromuscular process controlling balance	nitric-oxide synthase binding	nitric-oxide synthase regulator activity	Notch signaling pathway	N-terminal myristoylation domain binding	nucleic acid binding	oligosaccharide catabolic process	oxidation-reduction process	oxidoreductase activity	peptidyl-tyrosine phosphorylation	per a
Zymogen granule protein 16 homolog B		🟩																		
Secretoglobin family 1D member 2																				
Immunoglobulin lambda-like polypeptide 5																				
Alpha-amylase 2B																				
Immunoglobulin heavy constant alpha 1																				
1,4-alpha-glucan-branching enzyme																				
Cadherin-23																				
SRC kinase signaling inhibitor 1																				
Integrin beta-1-binding protein 1								🟩					🟩							
Peroxiredoxin-4																	🟩	🟩		🟩
JNK1/MAPK8-associated membrane protein																				
Ganglioside GM2 activator									🟩	🟩						🟩				
Calmodulin-1											🟩	🟩		🟩						
Titin	🟩				🟩	🟩													🟩	
Protein FRG1			🟩	🟩			🟩													
Probable ATP-dependent RNA helicase															🟩					

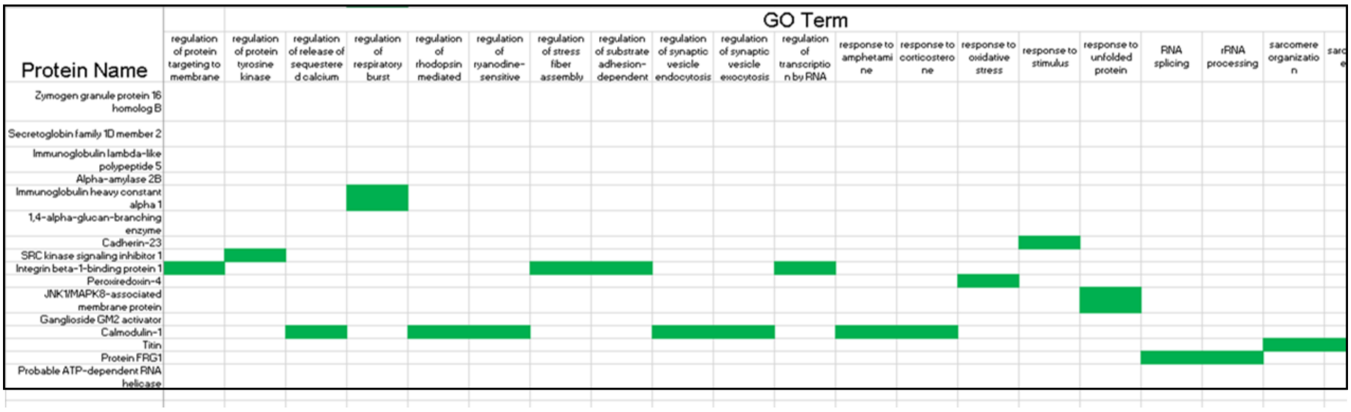


Protein Name	GO Term																			
	peroxidase activity	peroxiredoxin activity	phosphatidylinositol 3-kinase binding	phospholipase activator activity	phosphorylation	photoreceptor cell maintenance	protease binding	protein homodimerization activity	protein kinase A signaling	protein maturation by protein folding	protein N-terminus binding	protein phosphatase activator activity	protein phosphorylation	protein self-association	protein serine/threonine kinase activator	protein transport	protein transporter activity	protein tyrosine kinase activity	protein-chromophore linkage	Ras nu ex f
Zymogen granule protein 16 homolog B																				
Secretoglobin family 1D member 2																				
Immunoglobulin lambda-like polypeptide 5																				
Alpha-amylase 2B																				
Immunoglobulin heavy constant alpha 1																			🟩	
1,4-alpha-glucan-branching enzyme																				
Cadherin-23						🟩														
SRC kinase signaling inhibitor 1																				
Integrin beta-1-binding protein 1																🟩	🟩			
Peroxiredoxin-4	🟩	🟩						🟩		🟩										
JNK1/MAPK8-associated membrane protein																				
Ganglioside GM2 activator				🟩																
Calmodulin-1			🟩								🟩	🟩			🟩					🟩
Titin					🟩		🟩		🟩				🟩	🟩				🟩		
Protein FRG1																				
Probable ATP-dependent RNA helicase																				

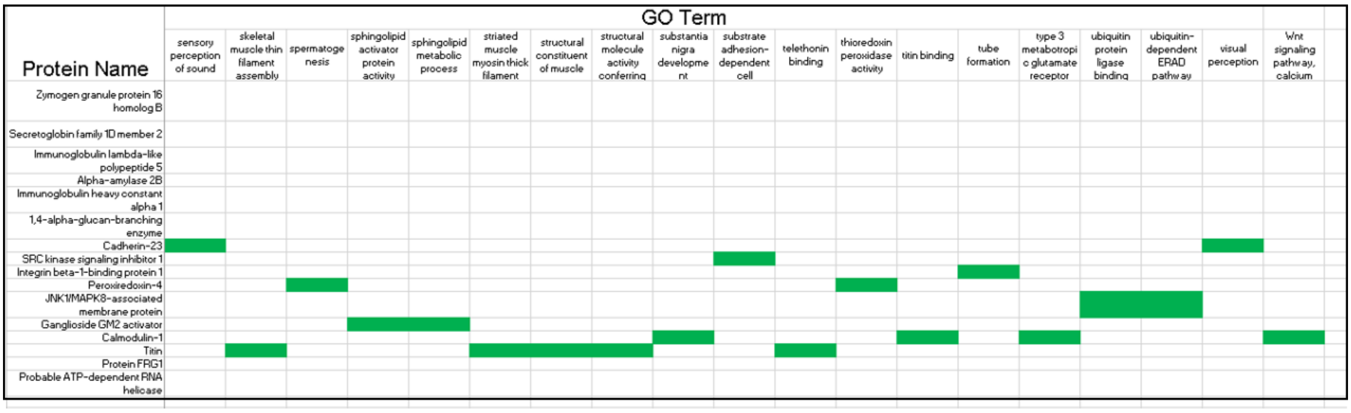
Supplementary Table 2 contd. Proteins identified from the LC-MS analysis and the molecular processes in which they are involved, as annotated on UniProt.org through phylogenetic-based propagation of functional gene ontology (GO) annotations.[2]



Protein Name	GO Term																			
	Ras guanyl-nucleotide exchange factor	reactive oxygen species metabolic	receptor clustering	receptor-mediated endocytosis	regulation by host of symbiont cAMP-	regulation of blood vessel size	regulation of cardiac muscle contraction	regulation of cardiac muscle contraction	regulation of catalytic activity	regulation of cell adhesion involved in	regulation of cell adhesion mediated by	regulation of cell communication by	regulation of cell division	regulation of cell migration involved in	regulation of cell proliferation	regulation of cyclic-nucleotide phosphodie	regulation of cytokinesis	regulation of cytosolic calcium ion concentrati	regulation of dendritic spine morphogen	reg end
Zymogen granule protein 16 homolog B																				
Secretoglobin family 1D member 2																				
Immunoglobulin lambda-like polypeptide 5																				
Alpha-amylase 2B																				
Immunoglobulin heavy constant alpha 1				🟩																
1,4-alpha-glucan-branching enzyme																				
Cadherin-23																		🟩		
SRC kinase signaling inhibitor 1																			🟩	🟩
Integrin beta-1-binding protein 1			🟩			🟩				🟩	🟩		🟩	🟩	🟩					
Peroxiredoxin-4		🟩																		
JNK1/MAPK8-associated membrane protein																				
Ganglioside GM2 activator																				
Calmodulin-1	🟩				🟩		🟩	🟩				🟩				🟩	🟩			
Titin									🟩											
Protein FRG1																				
Probable ATP-dependent RNA helicase																				



Protein Name	GO Term																			
	regulation of protein targeting to membrane	regulation of protein tyrosine kinase	regulation of release of sequestered calcium	regulation of respiratory burst	regulation of rhodopsin mediated	regulation of ryanodine-sensitive	regulation of stress fiber assembly	regulation of substrate adhesion-dependent	regulation of synaptic vesicle endocytosis	regulation of synaptic vesicle exocytosis	regulation of transcription by RNA	response to amphetamine	response to corticosterone	response to oxidative stress	response to stimulus	response to unfolded protein	RNA splicing	rRNA processing	sarcomere organization	sarc e
Zymogen granule protein 16 homolog B																				
Secretoglobin family 1D member 2																				
Immunoglobulin lambda-like polypeptide 5																				
Alpha-amylase 2B																				
Immunoglobulin heavy constant alpha 1				🟩																
1,4-alpha-glucan-branching enzyme																				
Cadherin-23															🟩					
SRC kinase signaling inhibitor 1		🟩																		
Integrin beta-1-binding protein 1	🟩						🟩	🟩			🟩									
Peroxiredoxin-4														🟩						
JNK1/MAPK8-associated membrane protein																🟩				
Ganglioside GM2 activator																				
Calmodulin-1			🟩		🟩	🟩			🟩	🟩		🟩	🟩							
Titin																			🟩	🟩
Protein FRG1																	🟩	🟩		
Probable ATP-dependent RNA helicase																				



Protein Name	GO Term																		
	sensory perception of sound	skeletal muscle thin filament assembly	spermatogenesis	sphingolipid activator protein activity	sphingolipid metabolic process	striated muscle myosin thick filament	structural constituent of muscle	structural molecule activity conferring	substantia nigra development	substrate adhesion-dependent cell	telethonin binding	thioredoxin peroxidase activity	titin binding	tube formation	type 3 metabotropic glutamate receptor	ubiquitin protein ligase binding	ubiquitin-dependent ERAD pathway	visual perception	Wnt signaling pathway, calcium
Zymogen granule protein 16 homolog B																			
Secretoglobin family 1D member 2																			
Immunoglobulin lambda-like polypeptide 5																			
Alpha-amylase 2B																			
Immunoglobulin heavy constant alpha 1																			
1,4-alpha-glucan-branching enzyme																			
Cadherin-23	🟩																	🟩	
SRC kinase signaling inhibitor 1										🟩									
Integrin beta-1-binding protein 1														🟩					
Peroxiredoxin-4			🟩									🟩							
JNK1/MAPK8-associated membrane protein																🟩	🟩		
Ganglioside GM2 activator				🟩	🟩														
Calmodulin-1									🟩				🟩		🟩				🟩
Titin		🟩				🟩	🟩	🟩			🟩								
Protein FRG1																			
Probable ATP-dependent RNA helicase																			

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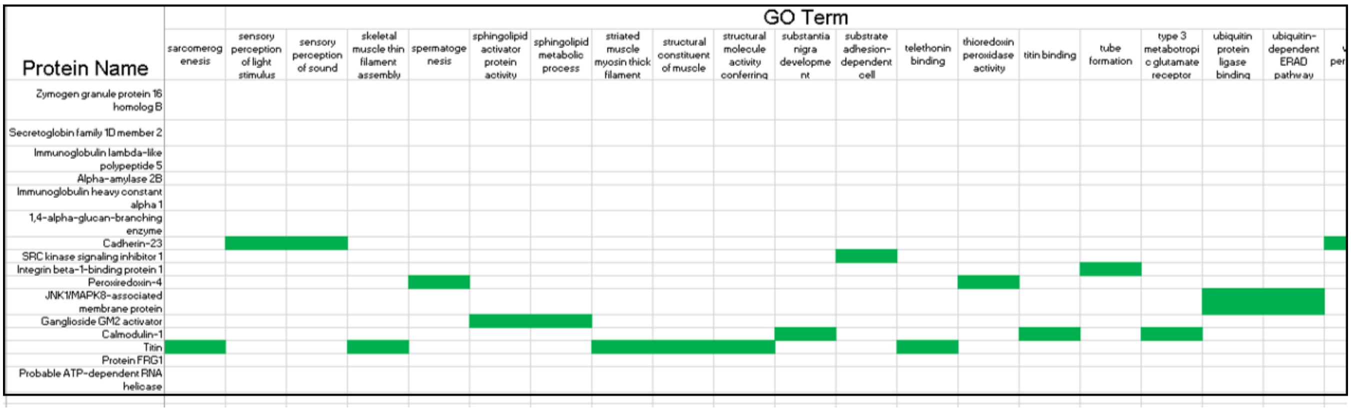
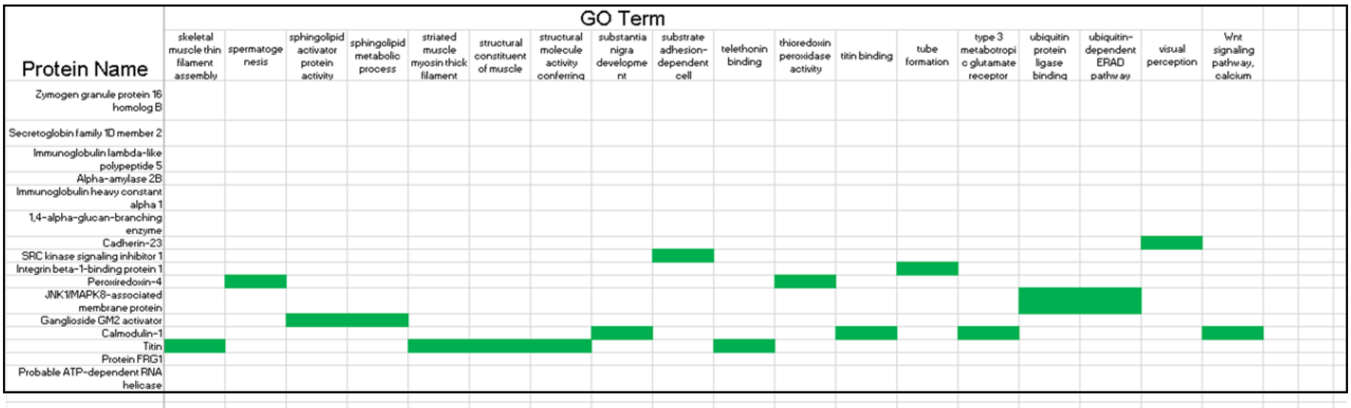
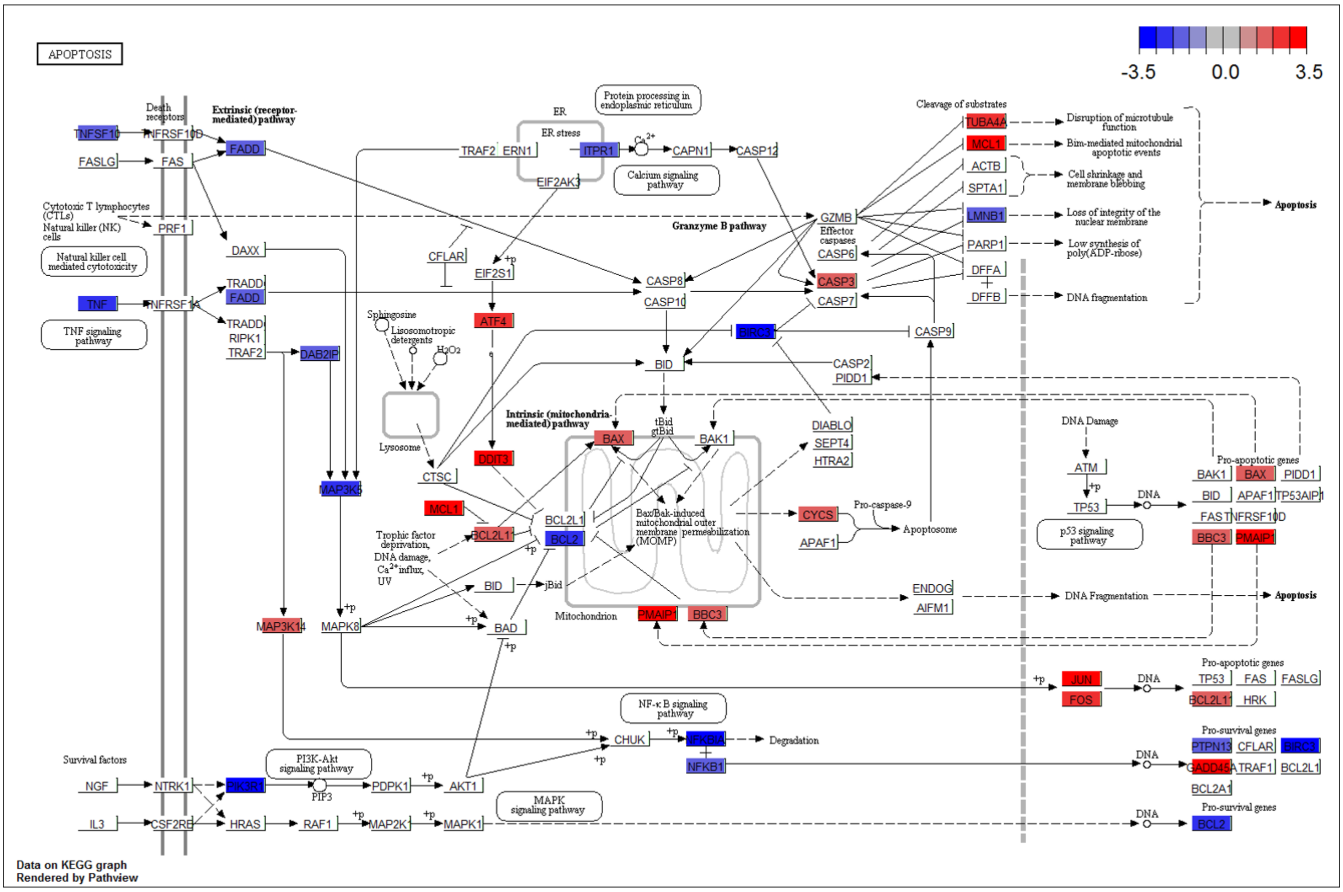


Protein Name	GO Term																			
	sarcomerogenesis	sensory perception of light stimulus	sensory perception of sound	skeletal muscle thin filament assembly	spermatogenesis	sphingolipid activator protein activity	sphingolipid metabolic process	striated muscle myosin thick filament	structural constituent of muscle	structural molecule activity conferring	substantia nigra development	substrate adhesion-dependent cell	telethonin binding	thioredoxin peroxidase activity	titin binding	tube formation	type 3 metabotropic glutamate receptor	ubiquitin protein ligase binding	ubiquitin-dependent ERAD pathway	v per
Zymogen granule protein 16 homolog B																				
Secretoglobin family 1D member 2																				
Immunoglobulin lambda-like polypeptide 5																				
Alpha-amylase 2B																				
Immunoglobulin heavy constant alpha 1																				
1,4-alpha-glucan-branching enzyme																				
Cadherin-23		🟩	🟩																	🟩
SRC kinase signaling inhibitor 1												🟩								
Integrin beta-1-binding protein 1																🟩				
Peroxiredoxin-4					🟩									🟩						
JNK1/MAPK8-associated membrane protein																		🟩	🟩	
Ganglioside GM2 activator						🟩	🟩													
Calmodulin-1											🟩				🟩		🟩			
Titin	🟩			🟩				🟩	🟩	🟩			🟩							
Protein FRG1																				
Probable ATP-dependent RNA helicase																				

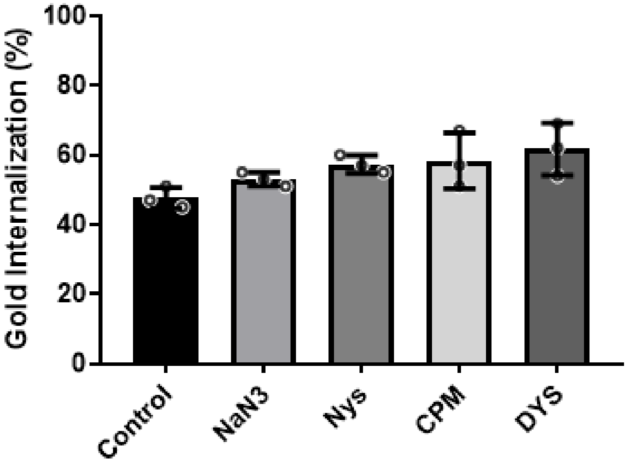


Protein Name	GO Term																	
	skeletal muscle thin filament assembly	spermatogenesis	sphingolipid activator protein activity	sphingolipid metabolic process	striated muscle myosin thick filament	structural constituent of muscle	structural molecule activity conferring	substantia nigra development	substrate adhesion-dependent cell	telethonin binding	thioredoxin peroxidase activity	titin binding	tube formation	type 3 metabotropic glutamate receptor	ubiquitin protein ligase binding	ubiquitin-dependent ERAD pathway	visual perception	Wnt signaling pathway, calcium
Zymogen granule protein 16 homolog B																		
Secretoglobin family 1D member 2																		
Immunoglobulin lambda-like polypeptide 5																		
Alpha-amylase 2B																		
Immunoglobulin heavy constant alpha 1																		
1,4-alpha-glucan-branching enzyme																		
Cadherin-23																	🟩	
SRC kinase signaling inhibitor 1									🟩									
Integrin beta-1-binding protein 1													🟩					
Peroxiredoxin-4		🟩									🟩							
JNK1/MAPK8-associated membrane protein															🟩	🟩		
Ganglioside GM2 activator			🟩	🟩														
Calmodulin-1								🟩				🟩		🟩				🟩
Titin	🟩				🟩	🟩	🟩			🟩								
Protein FRG1																		
Probable ATP-dependent RNA helicase																		

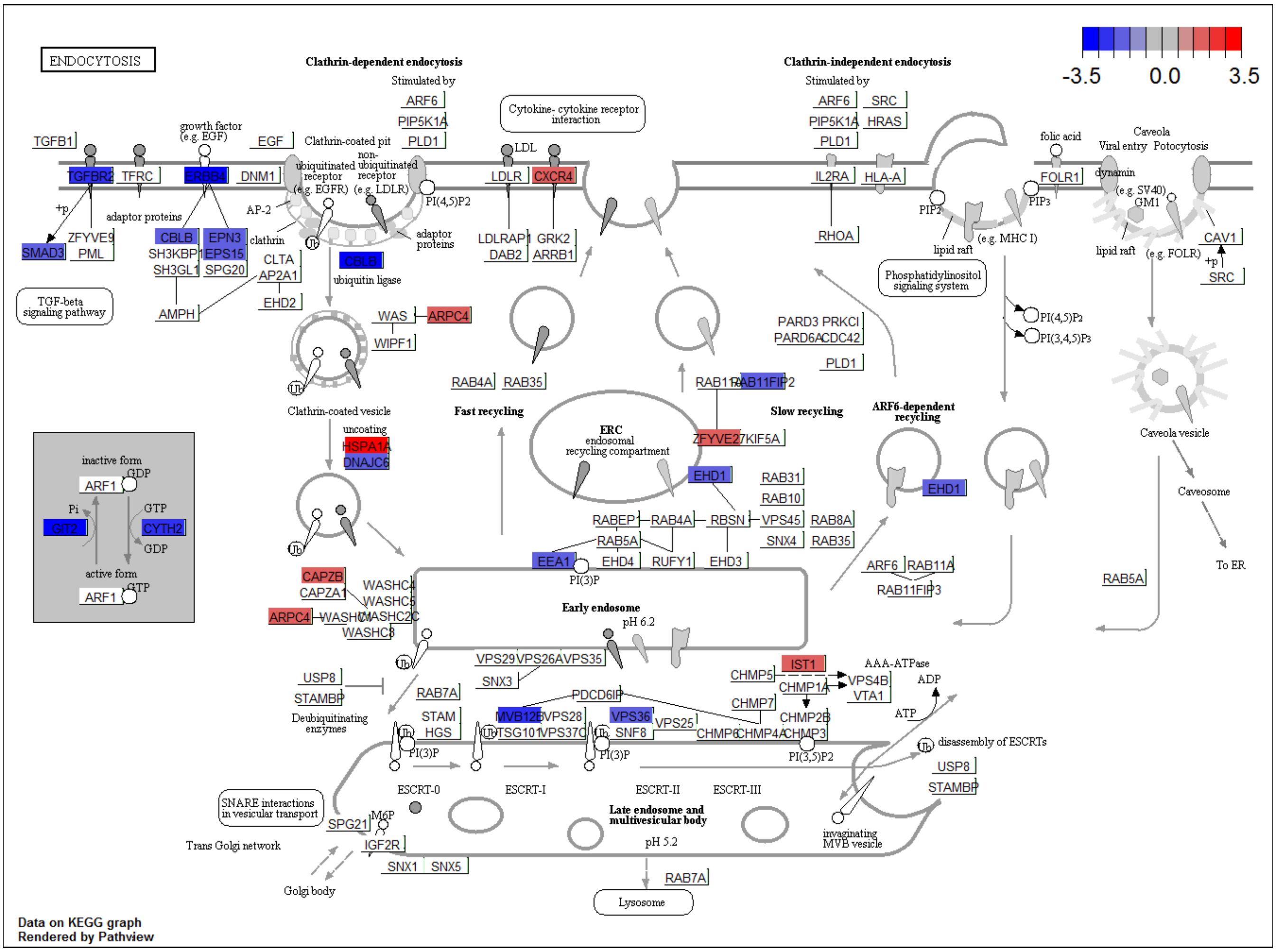
Supplementary Table 2 contd. Proteins identified from the LC-MS analysis and the molecular processes in which they are involved, as annotated on UniProt.org through phylogenetic-based propagation of functional gene ontology (GO) annotations.[2]



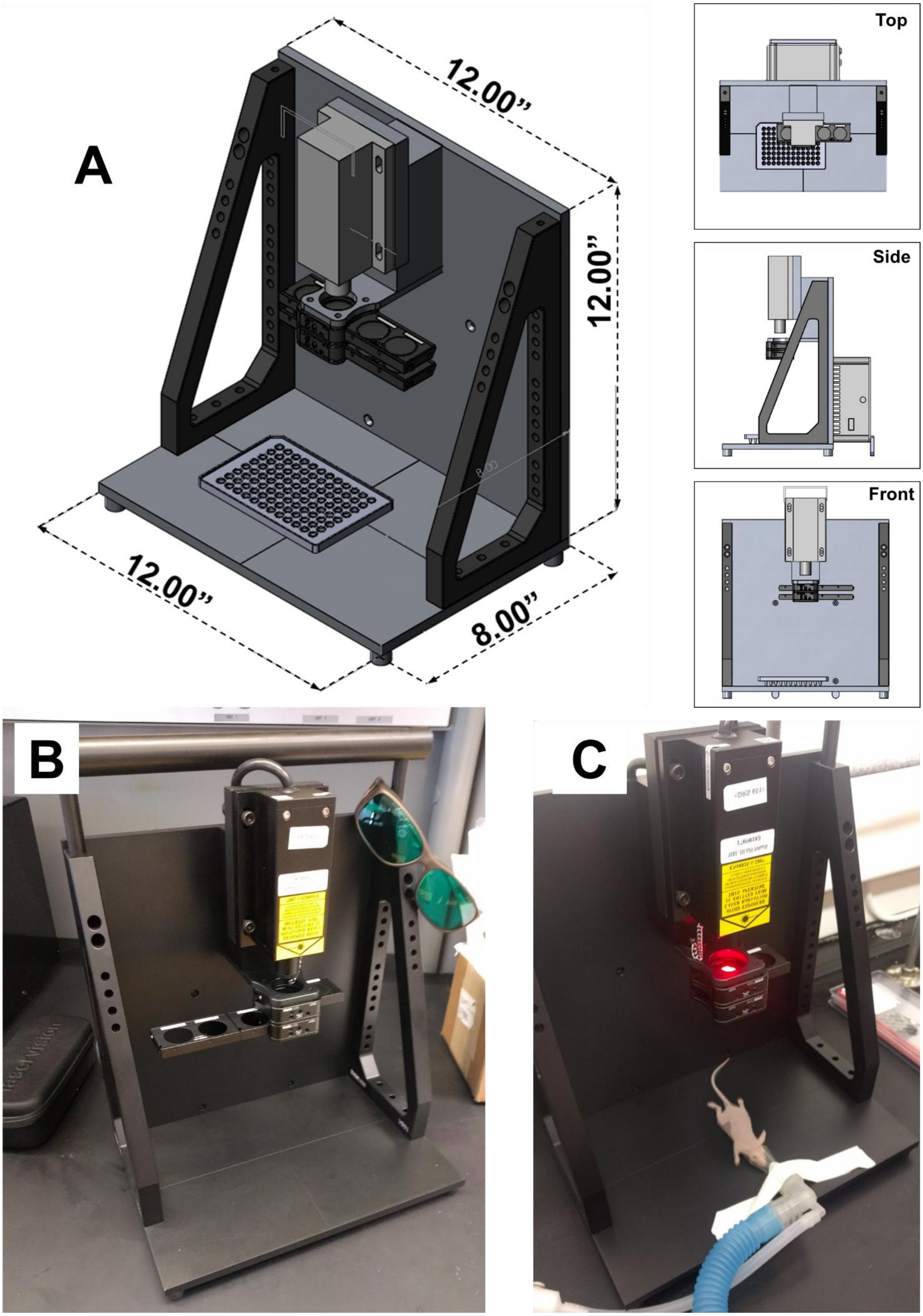
Supplementary Figure 5. Microarray based analysis for apoptosis related KEGG pathways for ionic gold treatment: Log-Fold-Change of gene regulation represented through apoptosis related KEGG pathways quantified through microarray analysis comparing Au-PEG treatments against untreated MCF-7 cells.



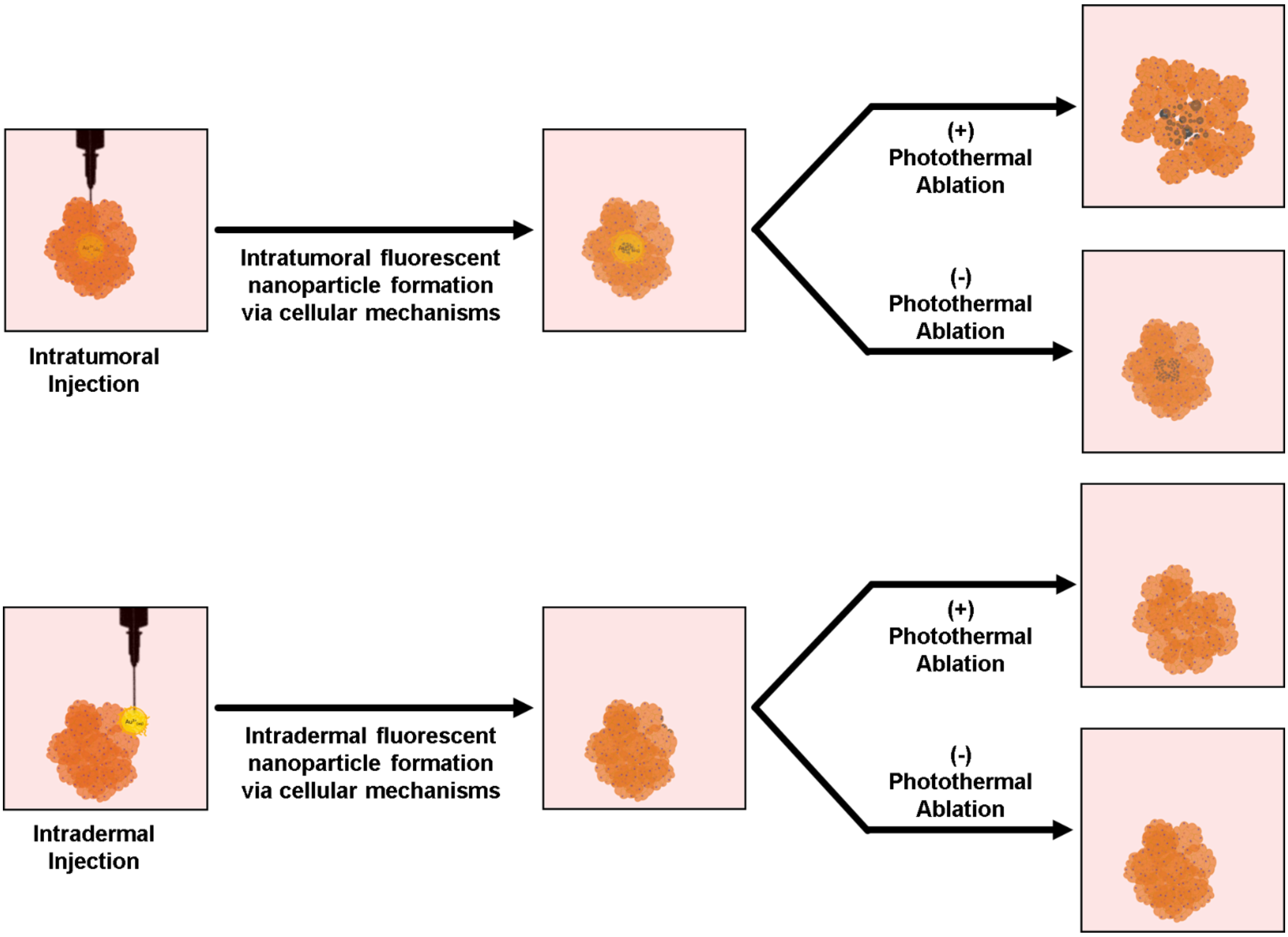
Supplementary Figure 6. Investigation of gold internalization pathway: Percentage of gold internalization in MCF-7 cells via application of ionic Au-PEG clusters at 0.24 mM Au^{3+}(control), or ionic Au-PEG clusters in presence of several endocytic inhibitors is shown. Different endocytic inhibitors employed in this study were sodium azide (NaN_3), 2-deoxyglucose, nystatin (Nys), chlorpromazine (CPM), and dynasore. Error bars are standard deviations of the mean (n=3 biologically independent samples).



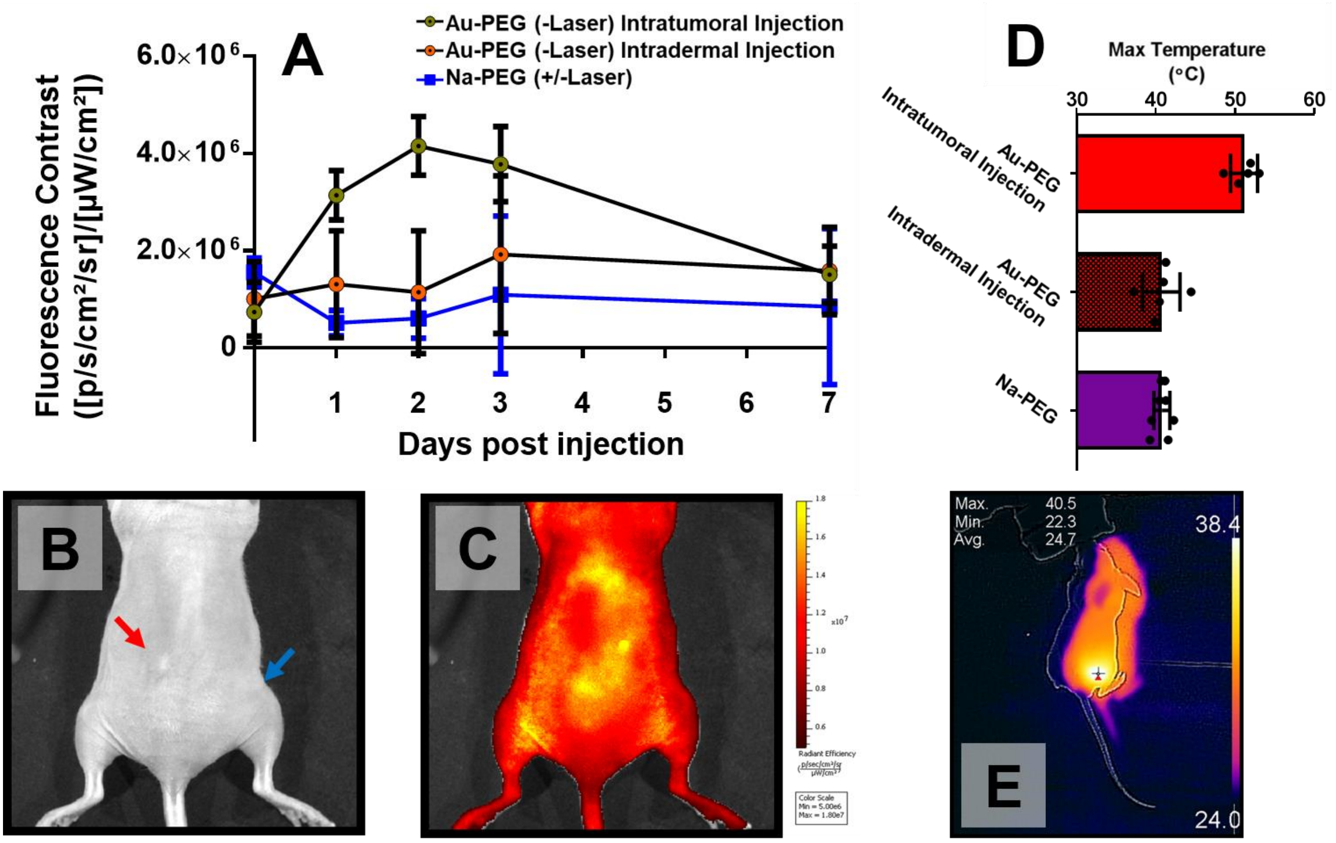
Supplementary Figure 7. Microarray based analysis for endocytosis related KEGG pathways for ionic gold treatment: Log-Fold-Change of gene regulation represented through endocytosis related KEGG pathways quantified through microarray analysis comparing Au-PEG treatments against untreated MCF-7 cells.


A
12.00”
12.00”
12.00”
8.00”
Top
Side
Front
B
C

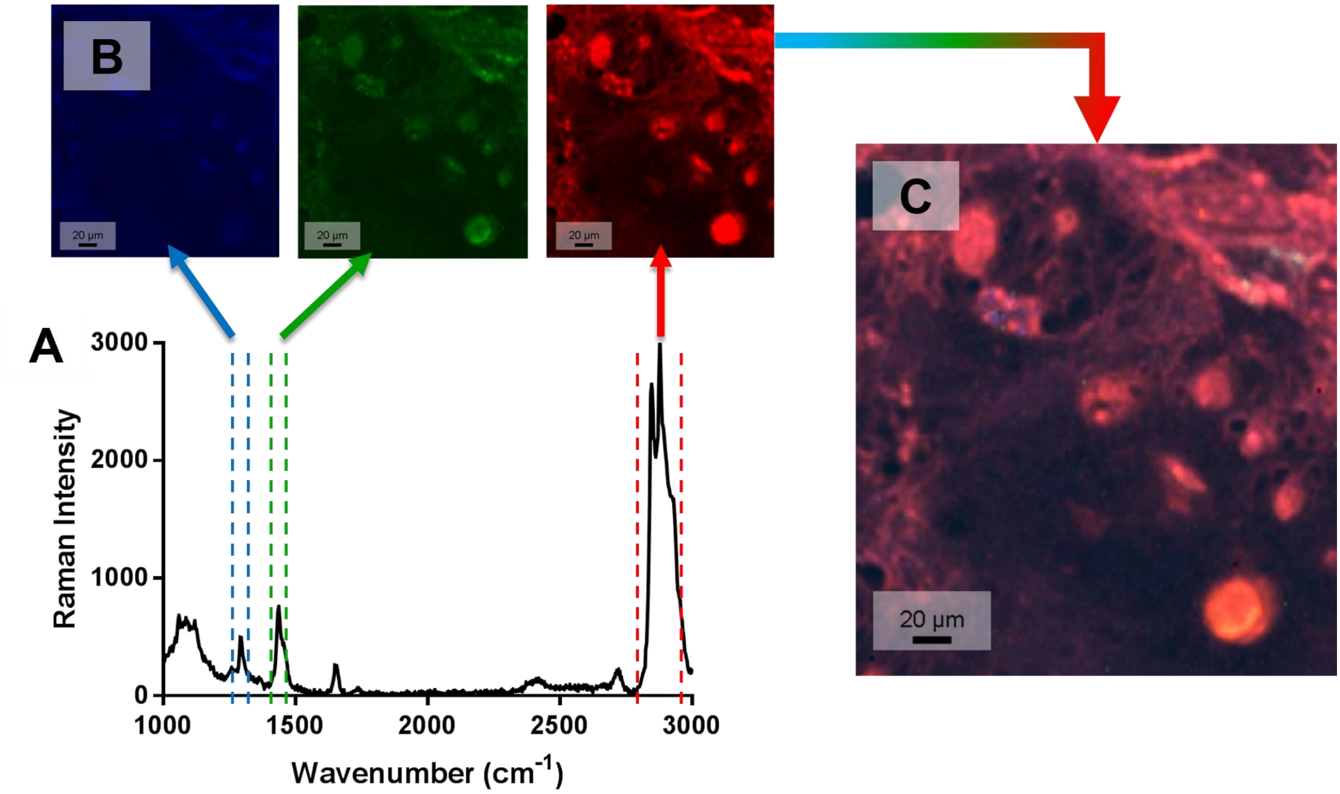
Supplementary Figure 8. Schematic set up for the photothermal ablation therapy: Computer-aided design (CAD) image of laser mount for photothermal ablative therapy (to scale with RTLMRL-635-500-5 Roithner Lasertechnik cw laser), with top, side, and front views (A). Image of complete setup (B). Image of laser setup with positioned mouse (C).



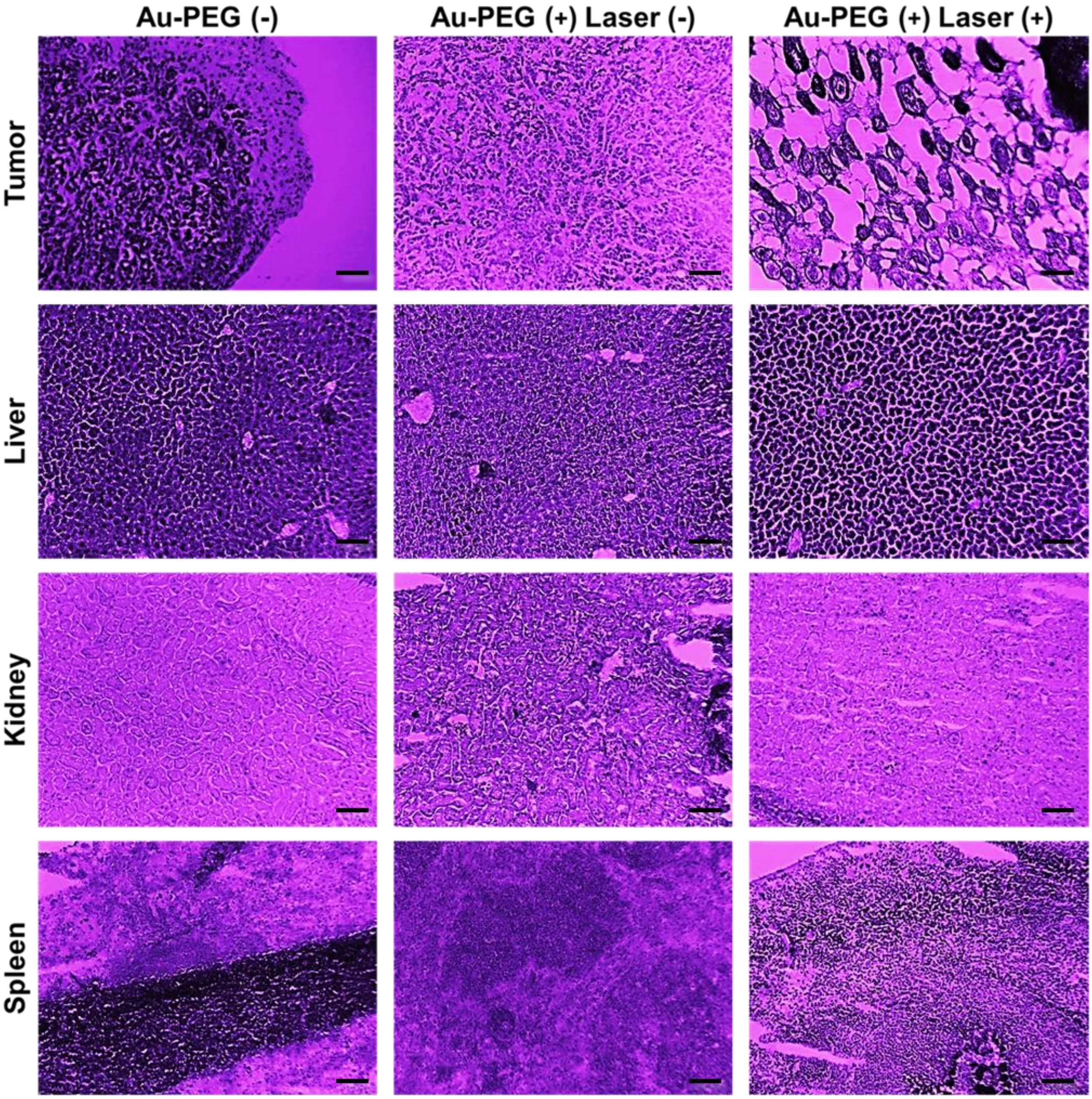
Supplementary Figure 9. Schematic diagram of nanoparticle formation: Artistic representation of how applications of ionic Au-PEG clusters will induce nanoparticle formation through successful intratumoral or intradermal applications with and without photothermal ablation.



Supplementary Figure 10. *In vivo* efficacy of the intratumorally generated gold nanoparticles: (A) Fluorescence contrast afforded via IVIS imaging (430_{Ex} 840_{Em}) between on-site and off-site across one week period of treatments for Au-PEG with no photothermal treatment with intratumoral injections (Yellow), Au-PEG with intradermal injections (Orange), or Na-PEG (Blue). Error bars are standard deviation of the mean (n ≥ 3 biologically independent animals). *The 1 day Au-PEG (-Laser) / Off site (Intradermal Injection) sample represents 2 biologically independent animals. Bright field (B) and fluorescence images (C) representitive of mice with Au-PEG with intradermal injection (three days post injection) with arrows indicating injection sites for either Na-PEG (Blue) or Au-PEG (Red). Temperature maximums averaged across laser treatments (D) as determined through FLIR IR thermal imaging with representitive thermal image of laser treatments made to mice with Au-PEG with intradermal injection (E). Error bars in for D are standard deviations of the mean (n ≥ 5 laser treatments).



Supplementary Figure 11. Raman mapping of gold nanoparticles: Illustration of how peak intensities for regions 1250-1350, 1446-1477, and 2849-2969 cm^{-1} (A) were used for generating Blue, Green, and Red color maps (B) and were then combined for Raman mapping of unstained histological sections (C).



Supplementary Figure 12. Evaluating *in vivo* toxicity: Representitive H&E stained tissue sections after microtomy from animals having received Au-PEG ± and/or laser treatments ± with Au-PEG. Scale bars are 100 μm.

Supplementary References.

1. Binder, J. X. *et al.* COMPARTMENTS: unification and visualization of protein subcellular localization evidence. *Database* **2014,** bau012-bau012 (2014).
2. Gaudet, P., Livstone, M. S., Lewis, S. E. & Thomas, P. D. Phylogenetic-based propagation of functional annotations within the Gene Ontology consortium. *Brief. Bioinform.* **12,** 449–62 (2011).