

Supplemental Information

Defining the human copper proteome and analysis of its expression variation in cancers

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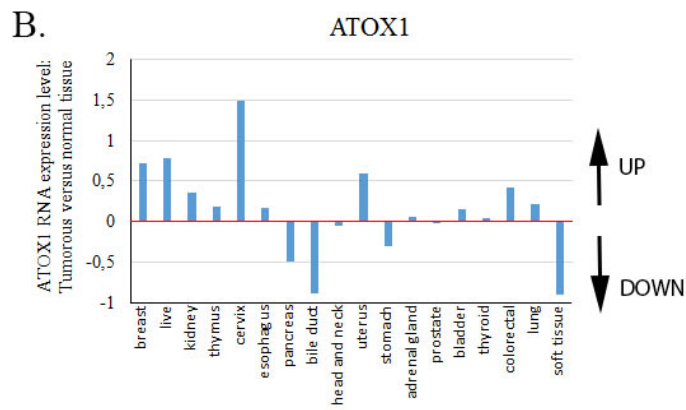
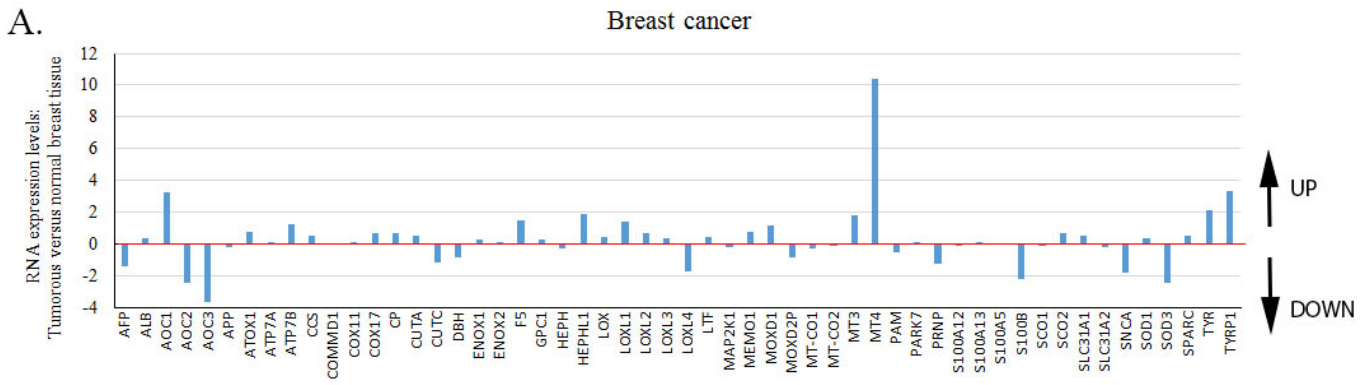
Table S1

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Supplementary Table 1:

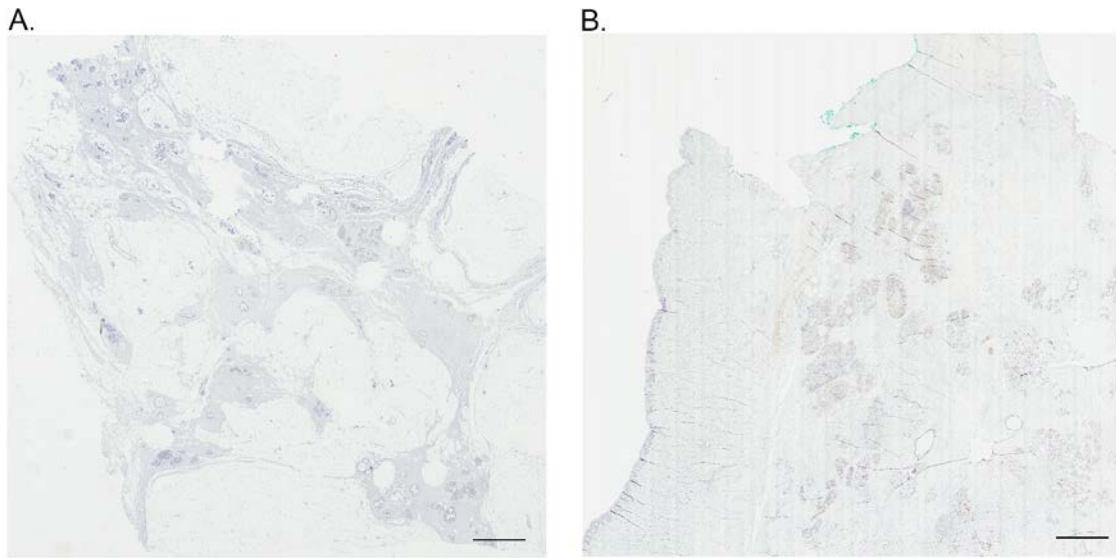
List of 54 genes that code for Cu-binding proteins in the human genome with approved gene symbols (common symbols), approved gene names, subcellular localization, protein function and tissue specificity.

Approved gene symbol (common symbol)	Approved gene name	Subcellular localization	Functionality	Tissue expression
ATOX1	Antioxidant 1 copper chaperone	Cytoplasm	Cu chaperone for Cu ATPases	all
CCS	Copper chaperone for superoxide dismutase	Cytoplasm	Cu chaperone for SOD1	all
COMM1D1	Copper metabolism domain containing 1	Nucleus, cytoplasm	Cu chaperone	all
COX11	COX11, cytochrome c oxidase copper chaperone	Mitochondria	Cu chaperone for COX	all
COX17	COX17, cytochrome c oxidase copper chaperone	Mitochondria	Cu chaperone / CCO targets	all
CUTC	CutC copper transporter	Nucleus, cytoplasm	Cu chaperone	all
SCO1	SCO1 cytochrome c oxidase assembly protein	Mitochondria	Cu chaperone	all
SCO2	SCO2 cytochrome c oxidase assembly protein	Mitochondria	Cu chaperone /COX1 Site A	all
ATP7A	ATPase copper transporting alpha	Golgi apparatus, cell membrane	Cu transporter (for e.g. PAM, TYR, LOX)	all, except liver
ATP7B	ATPase copper transporting beta	Golgi apparatus	Cu transporter	Tissue enriched (liver)
SLC31A1 (CTR1)	Solute carrier family 31 member 1	Cell membrane	Cu transporter/ plasma membrane uptake	all
SLC31A2 (CTR2)	Solute carrier family 31 member 2	Cell membrane	Cu transporter/ endosomal pump	Tissue enriched (salivary gland)/Mixed
AOC1	Amine oxidase, copper containing 1	Extracellular	Amine oxidase	Tissue enhanced (placenta) / Group enriched (colon, kidney, small intestine)
AOC2	Amine oxidase, copper containing 2	Cell membrane	Amine oxidase	Group enriched (adipose tissue, testis) / Mixed
AOC3	Amine oxidase, copper containing 3	Cell membrane	Amine oxidase	all
CP	Ceruloplasmin	Extracellular	Ferroxidase	Tissue enriched (liver)
HEPH	Hephaestin	Cell membrane	Ferroxidase	mixed
HEPHL1	Hephaestin like 1	Cell membrane	Ferroxidase	Group enriched (esophagus, tonsil) / Group enriched (cervix, uterine, esophagus, skin, vagina)
LOX	Protein-lysine 6-oxidase	Cell membrane	Ferroxidase	mixed
LOXL1	Lysyl oxidase homolog 1	Extracellular	Lysyl oxidase	mixed
LOXL2	Lysyl oxidase homolog 2	Extracellular	Lysyl oxidase	mixed
LOXL3	Lysyl oxidase homolog 3	Nucleus, extracellular	Lysyl oxidase	mixed
LOXL4	Lysyl oxidase homolog 4	Cytoplasm, extracellular	Lysyl oxidase	mixed
LOXL4	Lysyl oxidase homolog 4	Extracellular	Lysyl oxidase	mixed
MIT-CO1 (COX1)	Mitochondrially encoded cytochrome c oxidase I	Mitochondria	Oxidase	all
MIT-CO2 (COX2)	Mitochondrially encoded cytochrome c oxidase II	Mitochondria	Oxidase	all
TYR	Tyrosinase	Intracellular vesicles	Tyrosinase/oxidase	Tissue enriched (skin)
THRP1	Tyrosinase related protein 1	Intracellular vesicles	Oxidase	Tissue enhanced (heart muscle, skin) / Tissue enhanced (skin)
DBH	Dopamine beta-hydroxylase	Extracellular	Hydroxylase	Group enriched (adrenal gland, liver)
MAP2K1 (MEK1)	Dual specificity mitogen-activated protein kinase kinase 1	Nucleus, cytoskeleton, cytoplasm	Kinase	all
MEMO1	Mediator of cell motility 1	Cytosol, nucleus	Cu dependent redox protein	all
MOXD1	Monoxygenase DBH like 1	Endoplasmic reticulum	Monoxygenase	Tissue enhanced (endometrium, smooth muscle) / Tissue enhanced (endometrium)
MOXD2P	Monoxygenase, DBH-like 2, pseudogene	Endoplasmic reticulum	Monoxygenase	?
PAM	Peptidylglycine alpha-amidating monoxygenase	Cell membrane, extracellular	Monoxygenase	all
PAHR7	Parkinsonism associated deglycase	Nucleus, mitochondria, cell membrane	Deglycase	all
SOD1	Superoxide dismutase 1, soluble	Nucleus, cytoplasm	Dismutase	all
SOD3	Superoxide dismutase 3, extracellular	Extracellular	Dismutase	all
ENOX1	Ecto-NOX disulfide-thiol exchanger 1	Cell membrane, extracellular	Cu binding	mixed
ENOX2	Ecto-NOX disulfide-thiol exchanger 2	Cell membrane, extracellular	Cu binding	all
AFP	Alpha-fetoprotein	Extracellular	Cu binding	Tissue enriched (liver)
ALB	Serum albumin	Extracellular	Cu binding	Tissue enriched (liver)
APP	Amyloid beta A4 protein	Cell membrane	Cu binding	all
CUTA	cutA divalent cation tolerance homolog	Mitochondria	Cu binding	all
F5	Coagulation factor V	Extracellular	Cu binding	Group enriched (liver, gallbladder, placenta) / Tissue enriched (liver)
MT3	Metallothionein-3	Cytoplasm, Extracellular	Cu binding	Tissue enhanced (esophagus, skin) / group enriched (skin)
MT4	Metallothionein-4	Extracellular	Cu binding	Tissue enhanced (skin) / Al I
GPC1	Glypican 1	Cell membrane, extracellular	Cu binding	Tissue enhanced (bone marrow) / Tissue enriched (salivary gland)
LTF	Lactotransferrin	Nucleus, extracellular	Cu binding	all
PRNP	Prion protein	Nucleus, mitochondria, golgi apparatus, cell membrane, cytoplasm	Cu binding	Tissue enriched (bone marrow) / Group enriched (lung, spleen)
S100A12	S100 calcium binding protein A12	Cytoskeleton, cell membrane, cytoplasm, extracellular	Cu binding	all
S100A13	S100 calcium binding protein A13	Cytoplasm, extracellular	Cu binding	Tissue enhanced (thyroid gland)
S100A5	S100 calcium binding protein A5	Nucleus	Cu binding	Group enriched (adipose tissue, cerebral cortex) / All
S100B	S100 calcium binding protein B	Nucleus, cytoplasm	Cu binding	Tissue enhanced (bone marrow, cerebral cortex) / Group enriched (cerebellum, cerebral cortex, hippocampus)
SNCA	Synuclein alpha	Nucleus, cell membrane, cytoplasm, extracellular	Cu binding	all
SPARC	Secreted protein acidic and cysteine rich	Extracellular	Cu binding	all



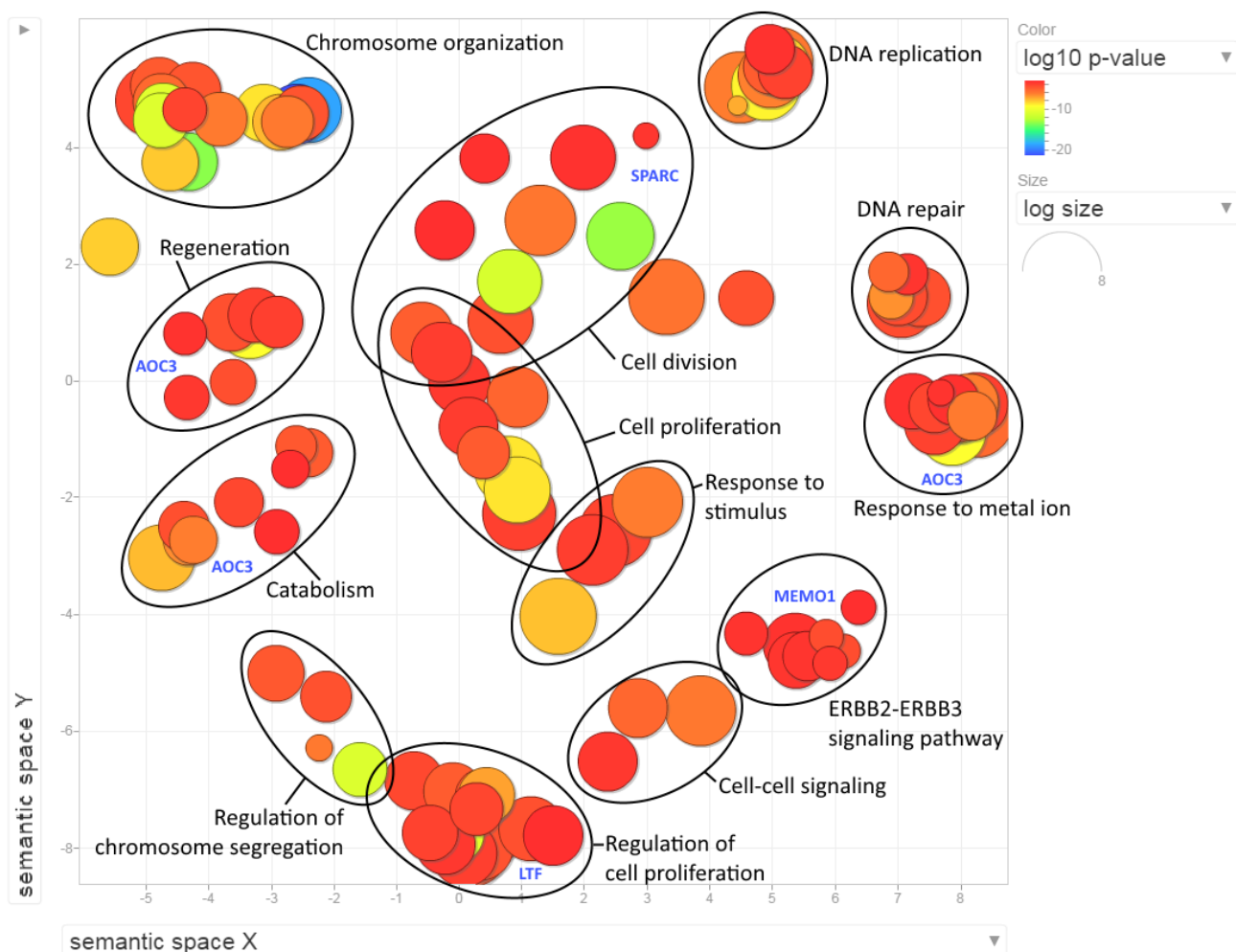
Supplementary Figure 1

A. Graph showing gene expression level of 54 genes in breast cancer. B. Graph showing protein expression level of ATOX1 in 18 cancer types.



Supplementary Figure 2

Benign (A) and tumorous (B) whole ductal breast tissue sections immunohistochemically stained for ATOX1. Scale bars indicate 2 mm.



Supplementary Figure 3

Scatterplot of clustered genes, showing overrepresentation in the Gene Ontology (GO) functional categories, generated using the ReviGO platform. Blue and green circles are GO terms with more significant p -values than the orange and red circles. The circles' x and y coordinates are derived by applying multidimensional scaling to a matrix of the GO terms' semantic similarities; therefore, their proximity on the plot reflects their closeness in the GO graph structure in terms of biological process (i.e. the semantic similarity). Over- or under-represented Cu-binding genes that are directly associated with the enriched GO terms have their gene symbol in blue fonts inside the corresponding elliptical grouping mark.