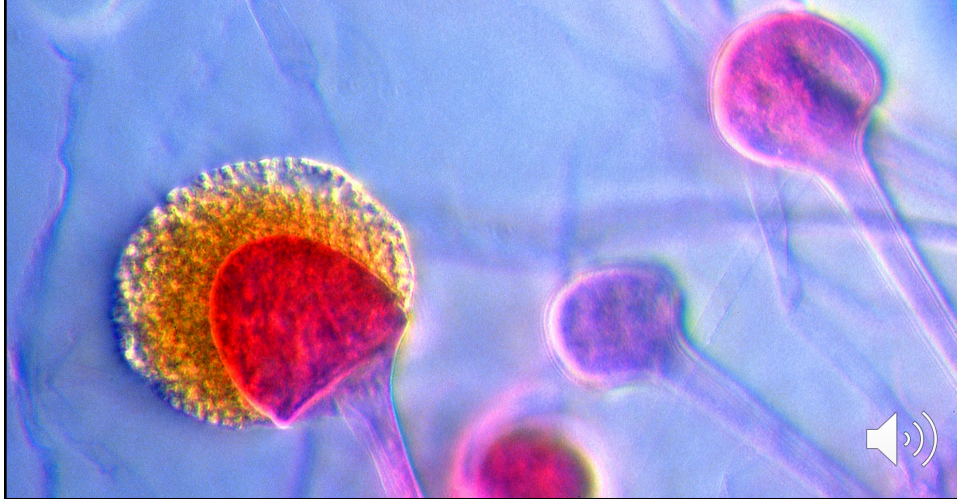# Correlations to Molecular Hypometabolism

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Disclosures

James Ryan is a principal in Progene DX, a company that sells the transcriptomic test called GENIE

Gene ExpressioN: Inflammation Explained

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Ribosome Large Subunit - CV

Subunit	CV
RPL	0.40
RPL	0.35
RPL	0.34
RPL	0.33
RPL	0.31
RPL	0.29
RPL	0.29
RPL	0.27
RPL	0.26

3

Ribosomes Sorted t-test – CD Markers

Gene	CD3D	CD127	CD25	CD4
Delta Z	1.95	1.32	1.23	-0.19
P value	4.8E-08	8.2E-04	4.4E-02	5.7E-01

Gene	CD14	CD40LG	CD48	CD52
Delta Z	-1.31	1.13	2.17	1.96
P value	2.6E-03	1.2E-01	5.0E-06	1.4E-08

4
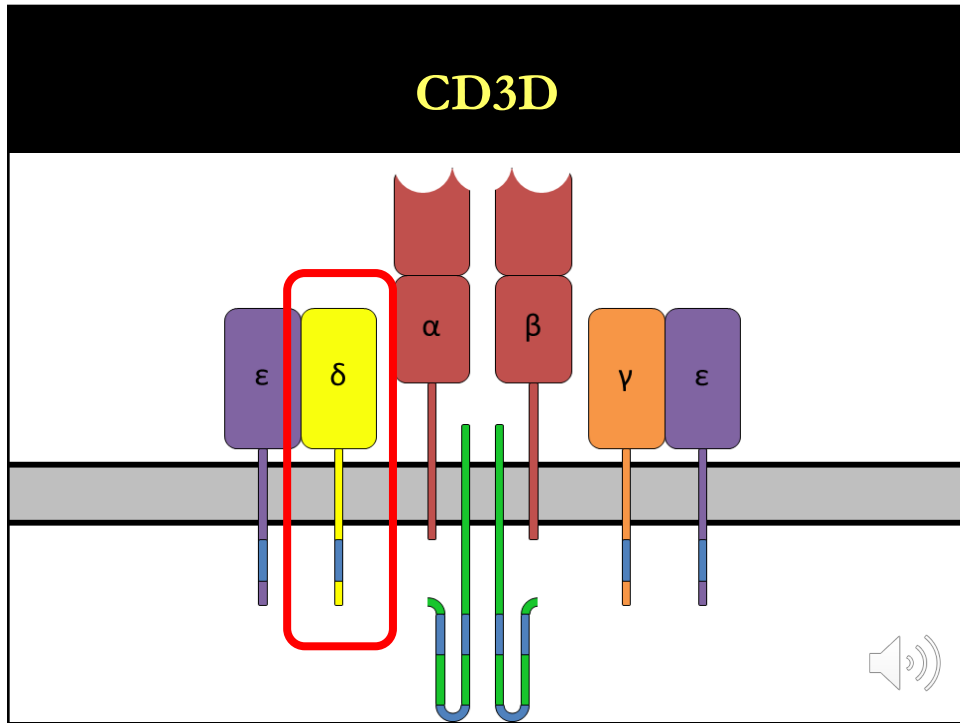
CD3D

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CD3D Sorted - SANS METABOLISM

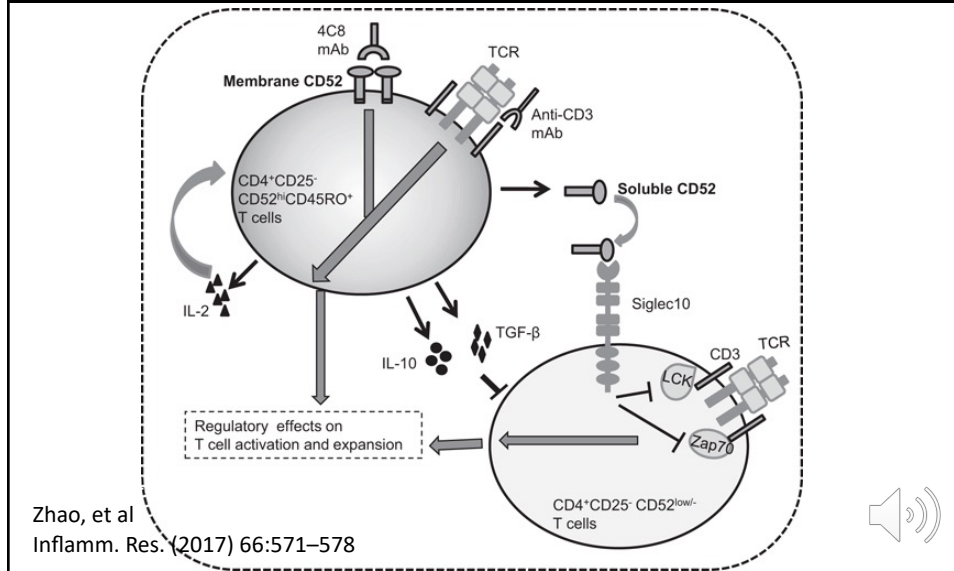|	
CD40LG	1.4E-22
CD52	2.8E-30
CD127	2.8E-26
HIF1a	1.2E-22
IQSEC1	2.3E-25
MAP3K5	5.8E-27
MAPK9	1.4E-33
STAT3	3.1E-33

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CD40LG
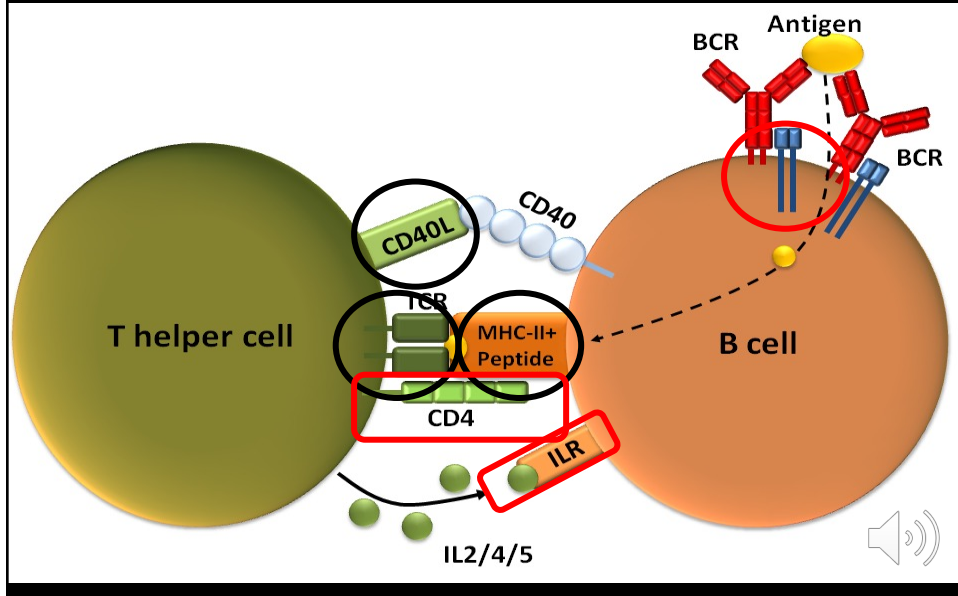
7

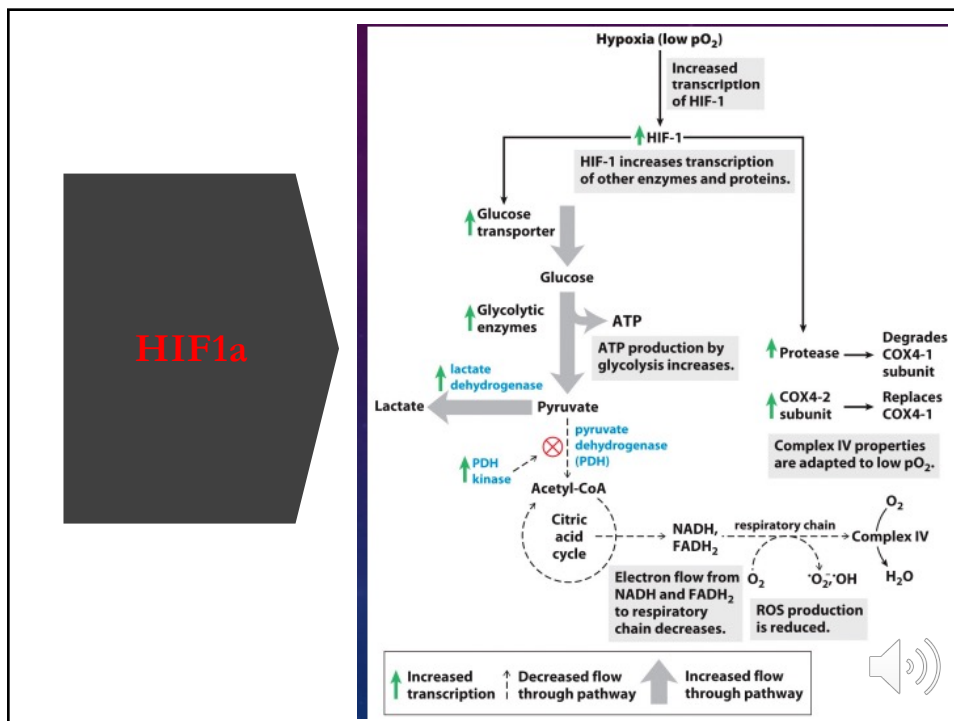CD40/CD40L checkpoint molecules interaction, Tang et al, **Pharmacol Ther. 2021 March ; 219: 107709**

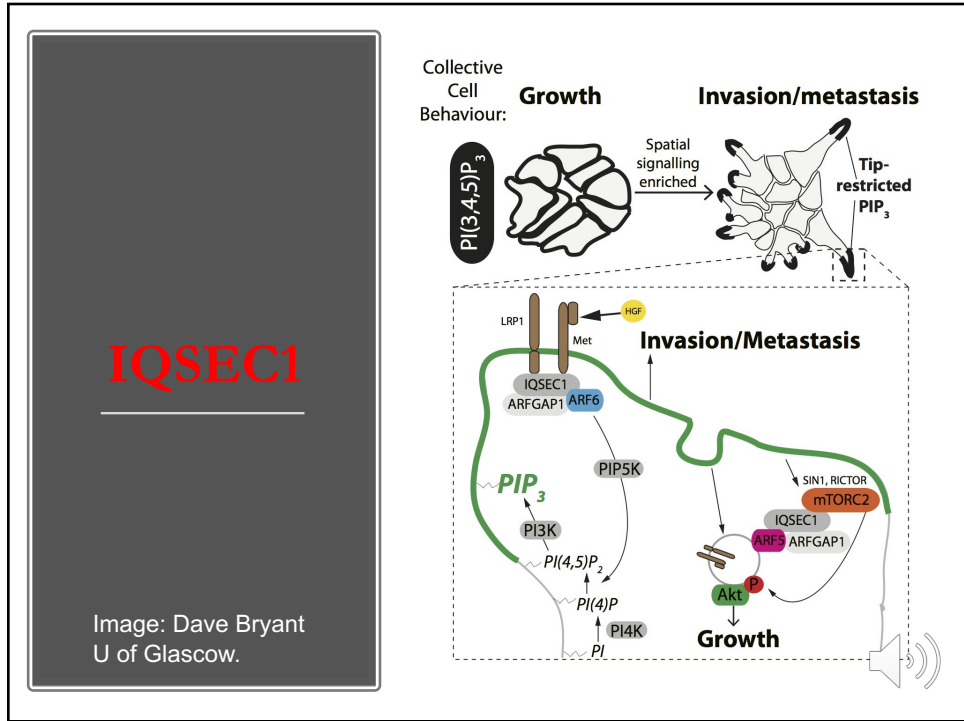| CD40L source	CD40 source	Effector function	Immunological process	PMID
TC	BC	BC proliferation, survival, differentiation, Ab production, IgD/M to IgA/G/E switching, memory response & costimulatory activity ↑	TC-dependent humoral immunity; Cellular immunity	27573866 29669250 7533092
Mast cell ILC Neutrophil NK cell	BC	BC proliferation, differentiation, Ab production, IgD/M to IgA/G/E switching & memory response↑	TC-independent humoral immunity	20101023 24562309 22197976 17630353
TC Platelet	MC/MΦ	MC/MΦ differentiation, costimulatory activity, cytokine production & anti-microbial activity ↑; MC apoptosis↓; TC Th1 response, CD8+ CTL response & memory CTL maintenance↑	Cellular immunity	15100268, 7594496 7843250, 8929557 27554817,8627184 10810999
TC Platelet	DC	DC maturation, proliferation, costimulatory activity & cytokine production↑; DC apoptosis↓; TC Th1 response, CD8+ CTL response & memory CTL maintenance↑	Cellular immunity	12893749 22154528 32453421 20811042
TC Platelet	Neutrophil	Oxidative burst & anti-microbial activity ↑	Cellular immunity	29518426 23785403
TC	Platelet	Platelet activation & release of RANTES↑	Thrombosis	14764664
TC Platelet	EC	EC IL-8, MCP-1 & adhesion molecules↑	Tissue inflammation	7500031 9468137
TC Platelet	VSMC	VSMC proliferation, MMPs & adhesion molecules↑	Tissue inflammation	9285647 28717419
TC	Fibroblast	Fibroblast IL6/8, RANTES & adhesion molecules↑; TC extravasation↑	Tissue inflammation	9144479
TC	KC	KC IL8, TNF-α & adhesion molecules↑	Tissue inflammation	8898941 8977185
TC	Epithelia	Epithelia IL6/8/15 & RANTES↑	Tissue inflammation	11053480, 11134253
TC Platelet	HPC	HPC proliferation, myeloid lineage differentiation & megakaryocytopoiesis↑	Myelopoiesis	9022082 9016882
Platelet	Platelet	Platelet activation↑	Thrombosis	12676820
Platelet	Leukocyte	Platelet-MC & platelet-neutrophil aggregates↑ Leukocyte extravasation↑	Thrombosis Tissue inflammation	12676820 27152726
TC	Tumor cell	Proliferation (malignant BC), IL-6, TNF-α costimulatory activity & apoptosis↑	Tumor cell fate	18497318,10068672 12070030, 9182676

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CD52 – aka Campath-1 antigen

Zhao, et al
Inflamm. Res. (2017) 66:571–578

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HIF1a

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IQSEC1

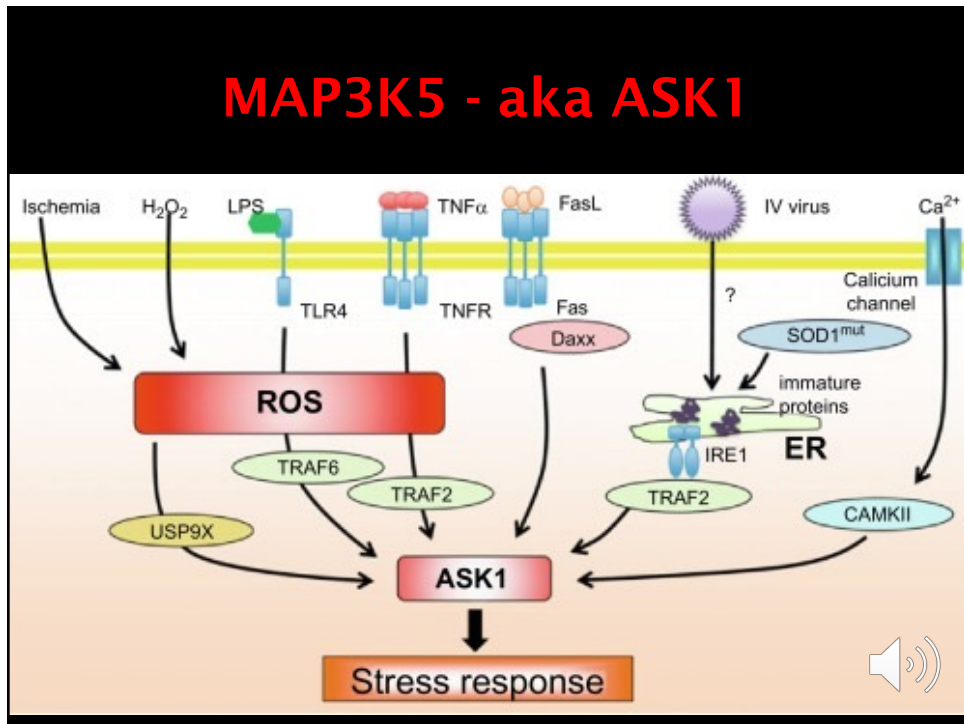Image: Dave Bryant
U of Glascow.

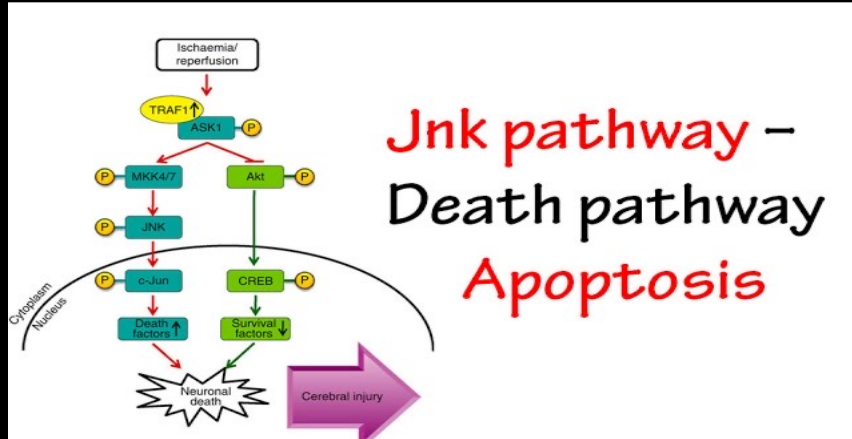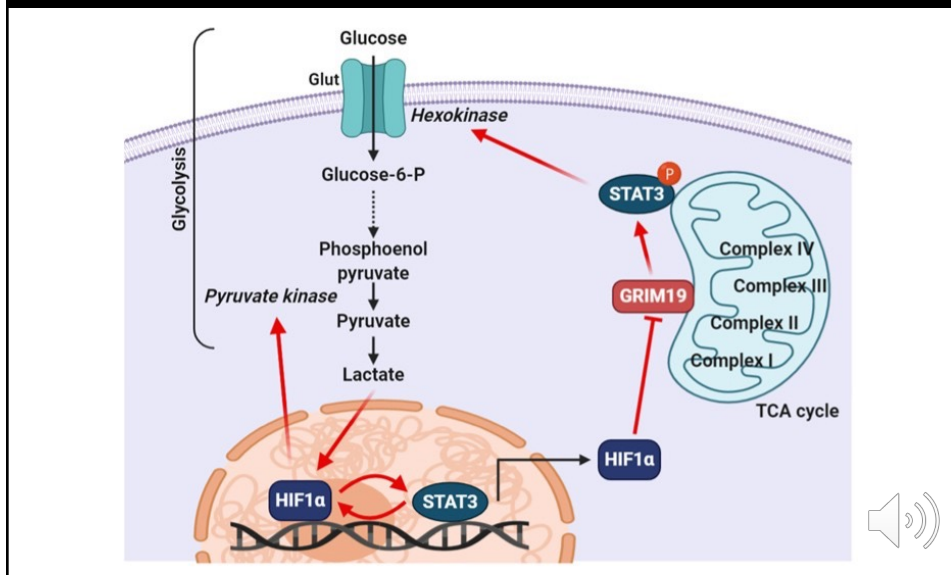11

MAP3K5 - aka ASK1

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MAPK9 – aka JNK2

13

STAT3

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Conclusions

- When we look at gene expression in CIRS, we can find interconnected networks by identifying expression patterns with strong correlations, both negative and positive

- When we looked into gene networks responding to suppressed metabolic activity, we found expression patterns in immune cells that are directly involved with both depressed adaptive immune function as well as networks important in metabolic reprogramming from oxidative phosphorylation to aerobic glycolysis.

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