

Pathways

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Family-Based Case-Control Study of IGF-1 PI: Elena Martinez

- Anthropometry, diet, other lifestyle factors and chronic hyperinsulinemia and CRC
- Candidate genotypes/haplotypes in genes involved in:
 - IGF-1 production
 - IGF-1 bioavailability
 - IGF-1 activityand CRC
- Interactions

Family-Based Case-Control Study of Folate Pathway

PI: Robert Haile

- Serine Hydroxymethyltransferase (SHMT1)
- Methylenetetrahydrofolate Reductase (MTHFR)
- Methionine Synthase (MTR)
- Methionine Synthase Reductase (MTRR)
- Thymidylate Synthase (TS)
- S-Adenosylhomocysteine Hydrolase (SAHH)
- Adenosine Deaminase (ADA)

Family-Based Case-Control Study of Folate Pathway

PI: Robert Haile

- Methionine Adenosyltransferase 2A (MAT2A)
- Folate Receptor (FOLR1)
- Reduced Folate Carrier (RFC1)
- S-Adenosylmethionine Decarboxylase (AMD1)
- Gastric Intrinsic Factor (GIF)
- Transcobalamin II (TCII)
- Intrinsic Factor Cobalamin Receptor (IFCR)
- Alcohol Dehydrogenase 3 (ADH3)

Family-Based Case-Control Study of Vitamin D and Calcium PI: Robert Haile

- Vitamin D receptor (VDR)
- Retinoid X Receptor (RXR)
- Vitamin D Binding Protein (DBP)
- Calcium Sensing Receptor (CaSR)
- Ileal sodium-dependent bile acid transporter (SLC10A2)

Family-Based Case-Control Study of Lipid Peroxidation PI: Manuela Gago

Oxidative stress-related genes:

- myeloperoxidase (MPO)
- endothelial cell nitric oxide synthase (ecNOS)
- manganese superoxide dismutase (MnSOD)
- selenium-dependent glutathione peroxidase (GPX1)
- phospholipid hydroperoxide glutathione peroxidase (GPX4)
- catalase (CAT)
- glutathione S-transferase A1 (GSTA1)

Family-Based Case-Control Study of Lipid Peroxidation PI: Manuela Gago

Oxidative stress-related genes (cont'd):

- glutathione S-transferase M1 (GSTM1)
- glutathione S-transferase T1 (GSTT1)
- glutathione S-transferase P1 (GSTP1)
- NAD(P)H:quinone oxidoreductase (NQO1)
- catechol-O-methyl transferase (COMT)
- paraoxonase 1 (PON1)
- heme oxygenase (HO1)
- peroxisome proliferator activated receptor gamma (PPAR γ)

in CRC

Family-Based Case-Control Study of Lipid Peroxidation PI: Manuela Gago

Modifying effects of these candidate genes on inverse associations between “protective factors”:

- marine n-3 fatty acids
- non-steroidal anti-inflammatory drugs (NSAIDs)
- physical activity
- dietary isothiocyanates
- vitamin D and calcium
- folate

and CRC

Family-Based Case-Control Study of Lipid Peroxidation PI: Manuela Gago

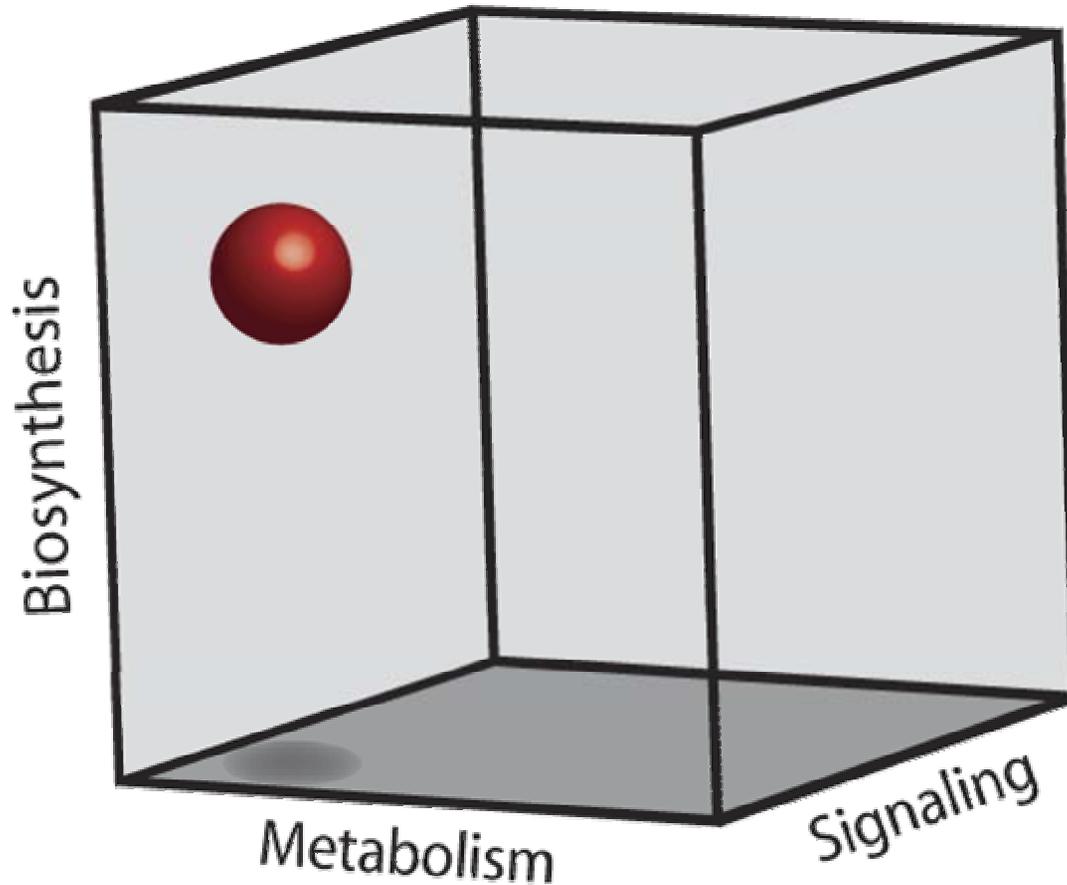
- Modifying effects of these candidate genes on association between alcohol intake and CRC
- Relationship of these candidate genes with plasma lipid peroxidation products among controls:
 - malondialdehyde, (MDA)
 - lipid peroxides
- Latent variable approach to association between plasma lipid-peroxidation products and CRC

Family-Based Case-Control Study of NSAIDs-Related Genes

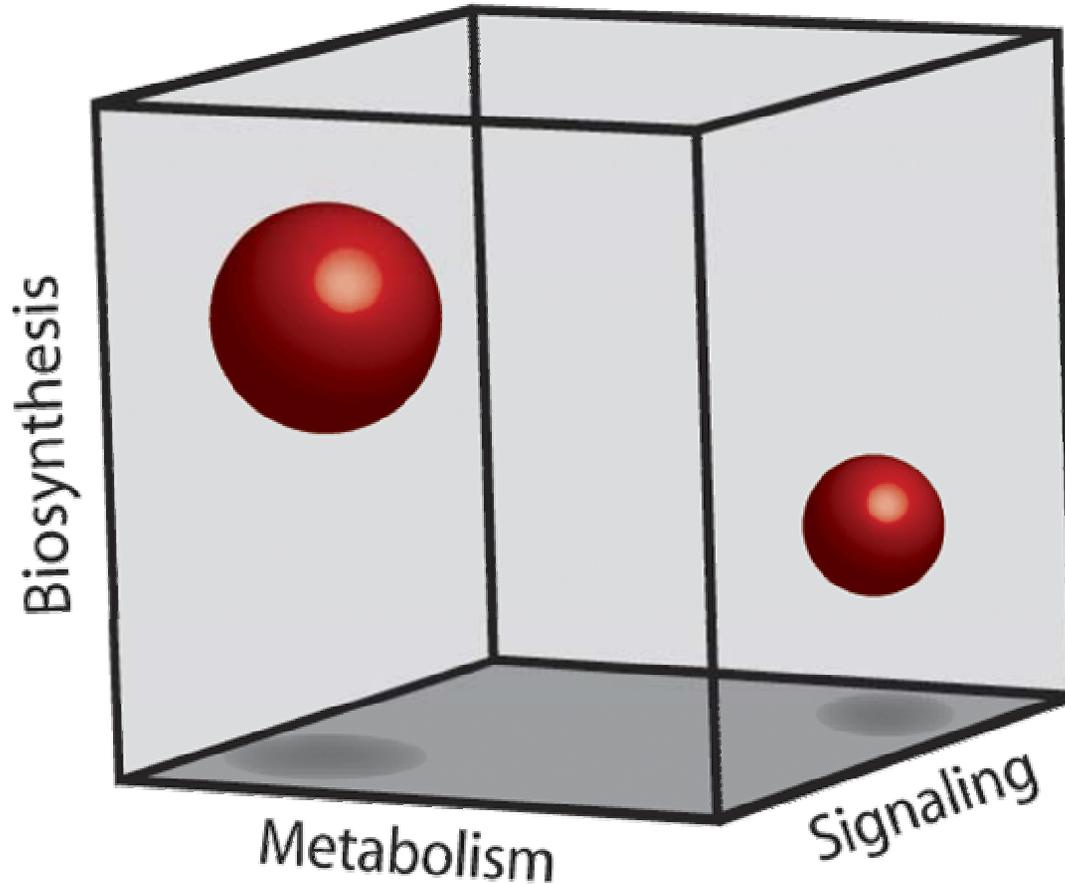
PI: John D. Potter

- Determine haplotypes for UGT1As, UGT2Bs, PTGS1, and PTGS2 in six ethnic groups
- Aspirin/NSAIDs use, polymorphisms in enzymes in aspirin/NSAIDs metabolism and prostaglandin synthesis, and CRC
- Functional studies of specificity of UGT1A and UGT2B isozymes for aspirin/NSAIDs, and the effect of polymorphisms on metabolism of NSAIDs

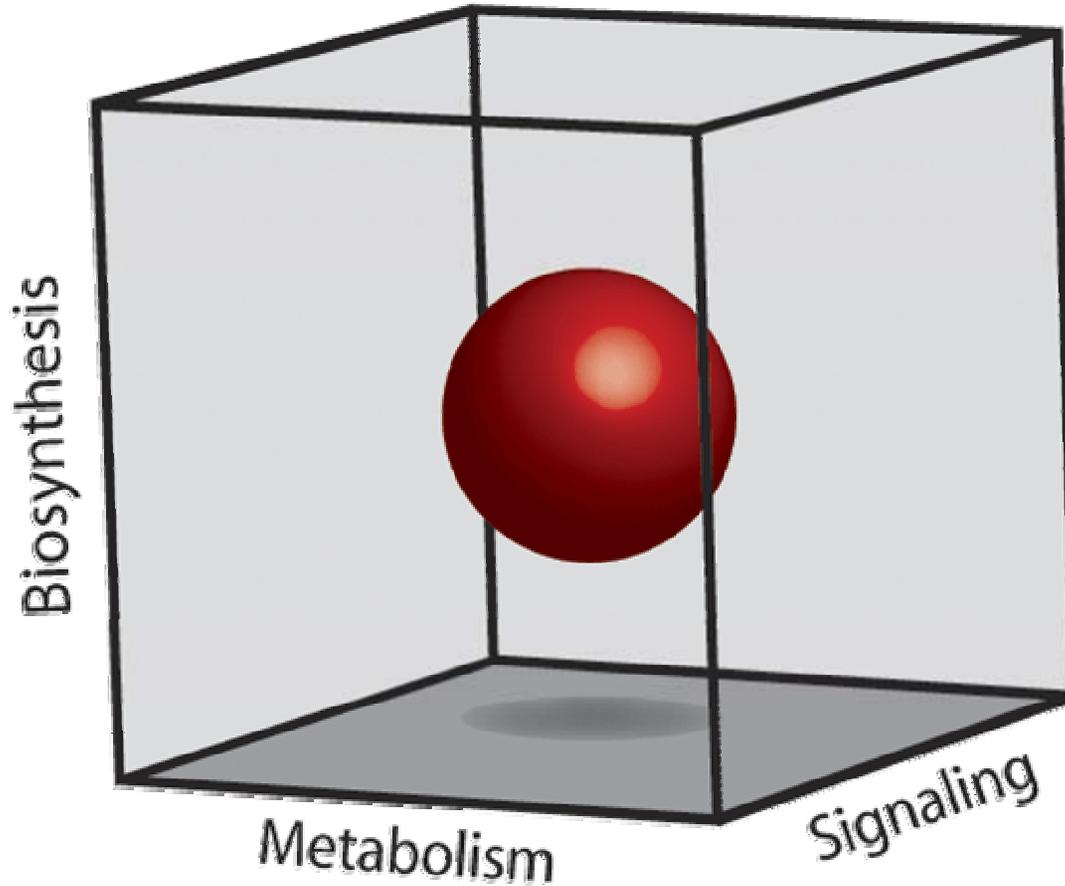
Possible and actual activity space for signaling pathways



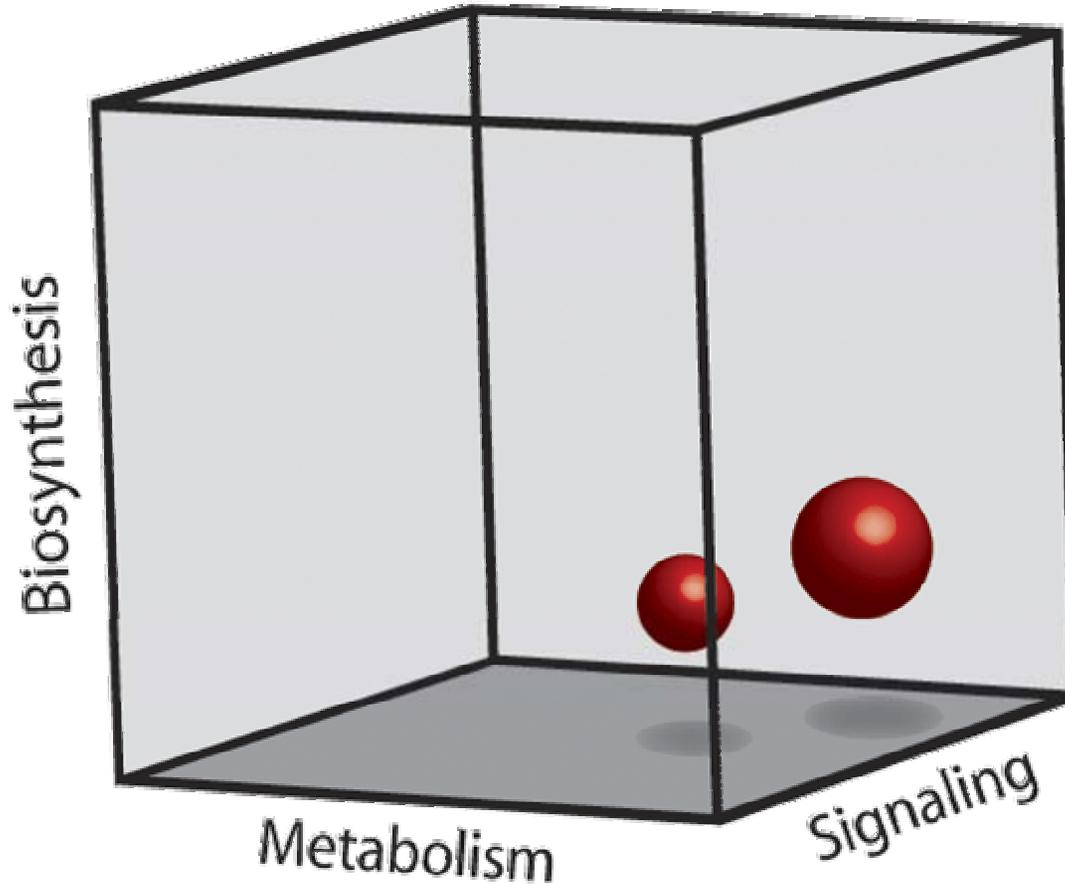
Signaling space with an active metabolite of primary



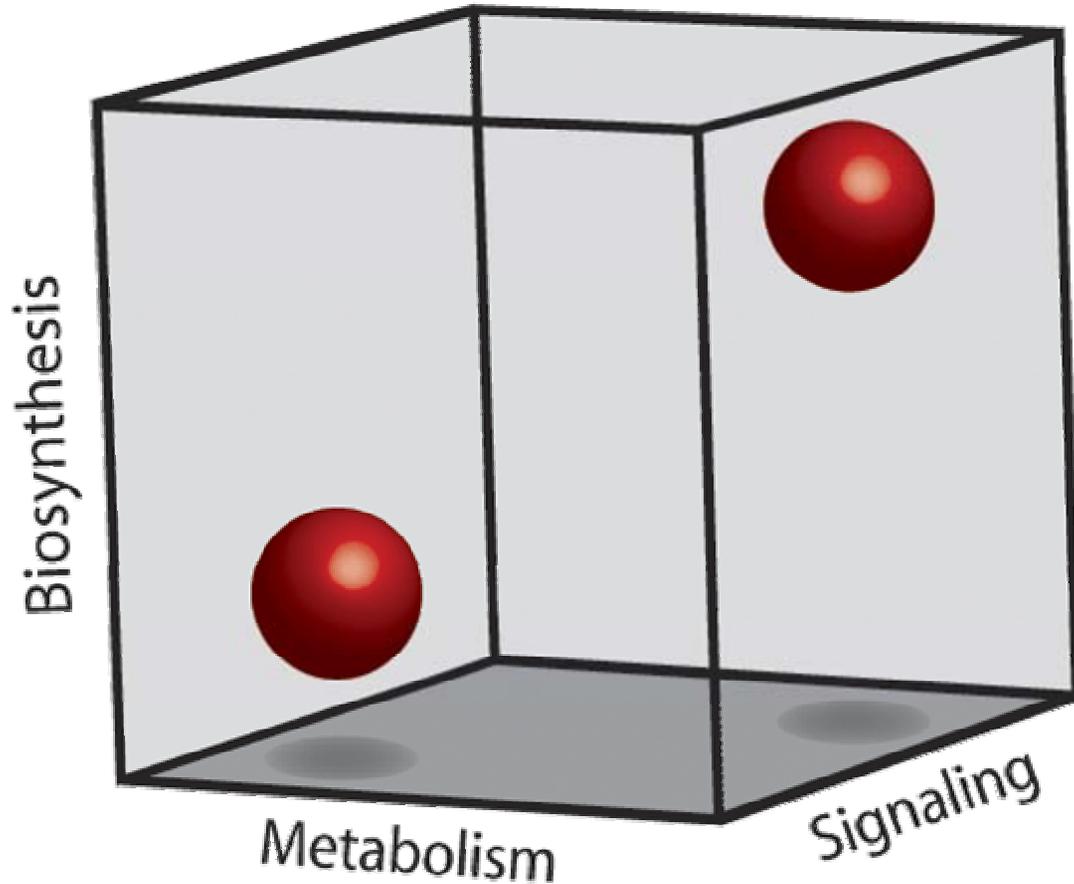
Signaling pathway state variation - diurnal; monthly; etc.



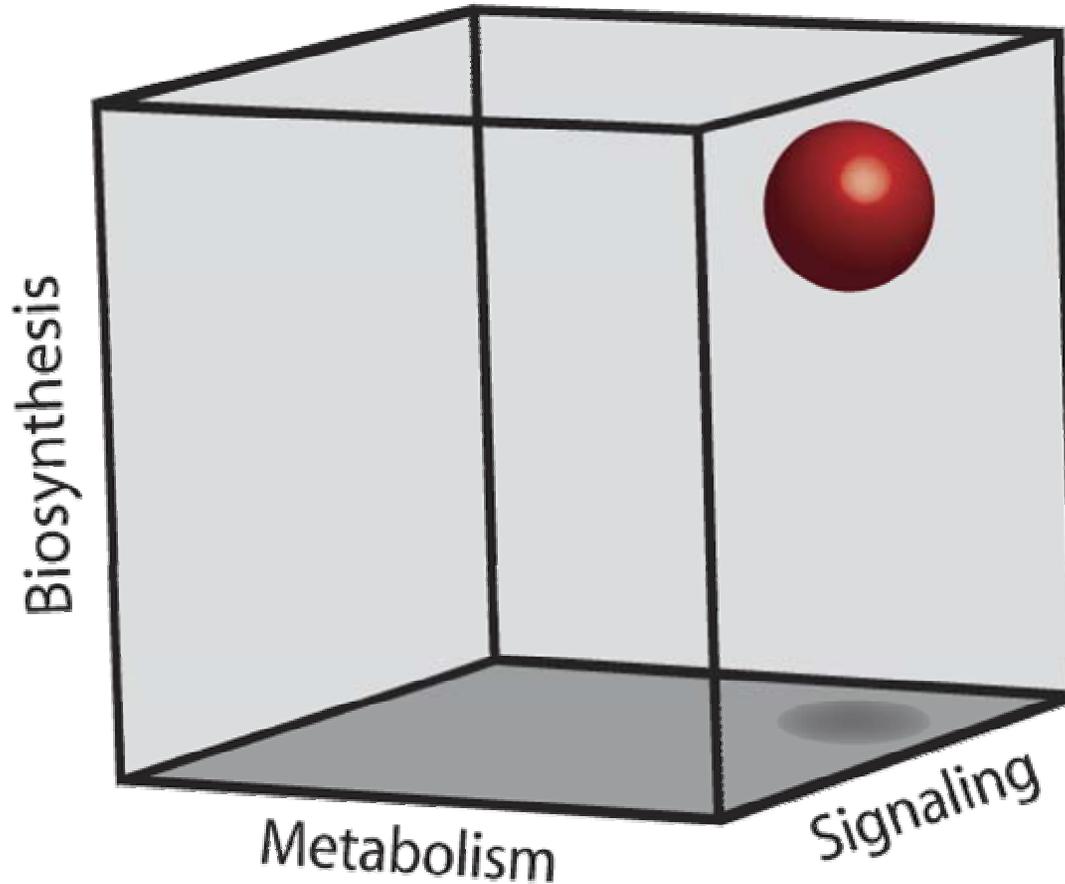
Signaling pathway switching: e.g. lifetime hormone states



Exogenous exposure: NSAIDs in prostaglandin signaling; PHM in hormone signaling; etc



Signaling Space in Tissue A



Signaling Space in Tissue B

