Approach - ***~Size of observation matrix***	**Tracer substrate**	**Applications** - ***Information***	**Advantages** - ***Biomarker***	**Disadvantages**	**Metabolites** - **Unidentified** ***Annotations***	**Bio-Informatics**
Targeted tracer fate association study (TTFAS) - ***~440 pathway functions/sample***	**Either (single)** **^{13}C-glucose** **or** **^{13}C- palmitate**	***In vitro, In vivo*** **Preclinical** **Investigational** - ***How homeostasis responds to a challenge***	**System-wide enzyme specific substrate-product relationships and response** - ***Flux driven surrogate (mechanistic) biomarkers of drug responsive multiple enzyme reactions***	**Tracer incubation, three conditions provide the least necessary associations, tracer cost**	**Common, abundant metabolic products and their isotopomers** - **None** ***None***	**Biochemist physicians with experience aid interpretations, Isotopomer associations require informatics tools**
Non-Targeted tracer fate detection (NTFD) - ***~190 labeled products/sample***	**Any tracer(s)** **^{13}C or Deuterium labeled substrates** **Such as glucose and/or $^{13}CO_2$**	***In vitro, In vivo*** **Preclinical** **Investigational** - ***New putative products***	**Substrate-product labeling via both exchange and new synthesis,** - ***Flux driven (non-mechanistic) markers of new synthesis***	**Tracer incubation, non-reaction specific new product labeling, isotope dilution**	**Common, abundant tracer labeled products** - **None** ***Minimal***	**Simple substrate to product real time labeling, Newly labeled fractions, informatics tools available**
Classic non-targeted non-tracer metabolomics - ***>600 metabolites/sample***	**None**	***In vitro, In vivo*** **Preclinical** **Investigational** **Clinical** **Population** - ***Metabolites present***	**All ranges of medical research and clinical applications** **Interdisciplinary** **Multiple center platforms** - ***Non-mechanistic principal components as potential markers***	**Incompatible platforms** **Individual variations and nutritional states greatly confuse interpretations**	**Preexisting, condition-related and consumed metabolic products** - **~50% unknowns** ***Significant effort***	**Heavy informatics (PCA)** ***Ad hoc* interpretations** **Uncertain clinical applicability**
Non-Targeted Mixed tracer - ***~200 pathway functions/sample***	**Multiple** **^{13}C or Deuterium labeled substrates** **Such as glucose, glutamine and/or palmitate**	***In vitro*** - ***Most possible new putative products of common substrates***	**Multiple substrate-product labeling via exchange and new synthesis** - ***Flux driven (non-mechanistic) markers of new synthesis***	**Tracer incubation, complex experimental design, versatile algorithms and simulations, drugs alter uptake of different tracers**	**Common, abundant non-tracer specific labeled products** - **None** ***None***	**Complex substrate to product real time labeling,** **Complex informatics tools** **Experience needed**
Non-Targeted Parallel multiple tracer - ***~200 pathway functions/sample***	**Parallel single** **^{13}C or Deuterium labeling studies of "identical" biological conditions**	***In vitro, In vivo*** **Preclinical** **Investigational** **Clinical** - ***Most possible new putative products of distinct substrates***	**Multiple substrate-product labeling via exchange and new synthesis** - ***Flux driven (non-mechanistic) markers of new synthesis***	**Tracer incubation, diverse biological conditions, drugs alter uptake of different tracers, cost of tracers and time**	**Common, abundant non-tracer specific labeled products** - **None** ***None***	**Complex interpretations due to differing experimental conditions in separate studies**
Precursor/Product isotope matching (PRISOMATCH) - ***Combined with specific antibody and electrophoresis separation methods***	**Single low enrichment** **^{13}C, Deuterium or ^{15}N** **Tracers are not necessary for natural isotope variation matching**	***In vitro, In vivo*** **Preclinical** **Investigational** **Clinical** **Population** - ***Product turnover optimized with disease state and drugs***	**Substrate-product labeling via exchange and new synthesis** - ***Disease/drug responsive tissue specific large molecule (sterols, peptide, protein, >m/z300) synthesis and turnover***	**Low abundance flexible time tracer incubation may be necessary** **Applicable only for larger (>30) carbon products (sterols, proteins, peptides)**	**Common, abundant non-tracer specific labeled products** **Antibody capturing gel electrophoresis improves specificity** - **None** ***None***	**Substrate-product real time labeling and turnover interpretations** **Clinical applications require physician biochemists**