EPA United States Environmental Protection Agency

Identifying Candidate Chemical-Disease Linkages

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Environmental and Epigenetic Determinants of IBD
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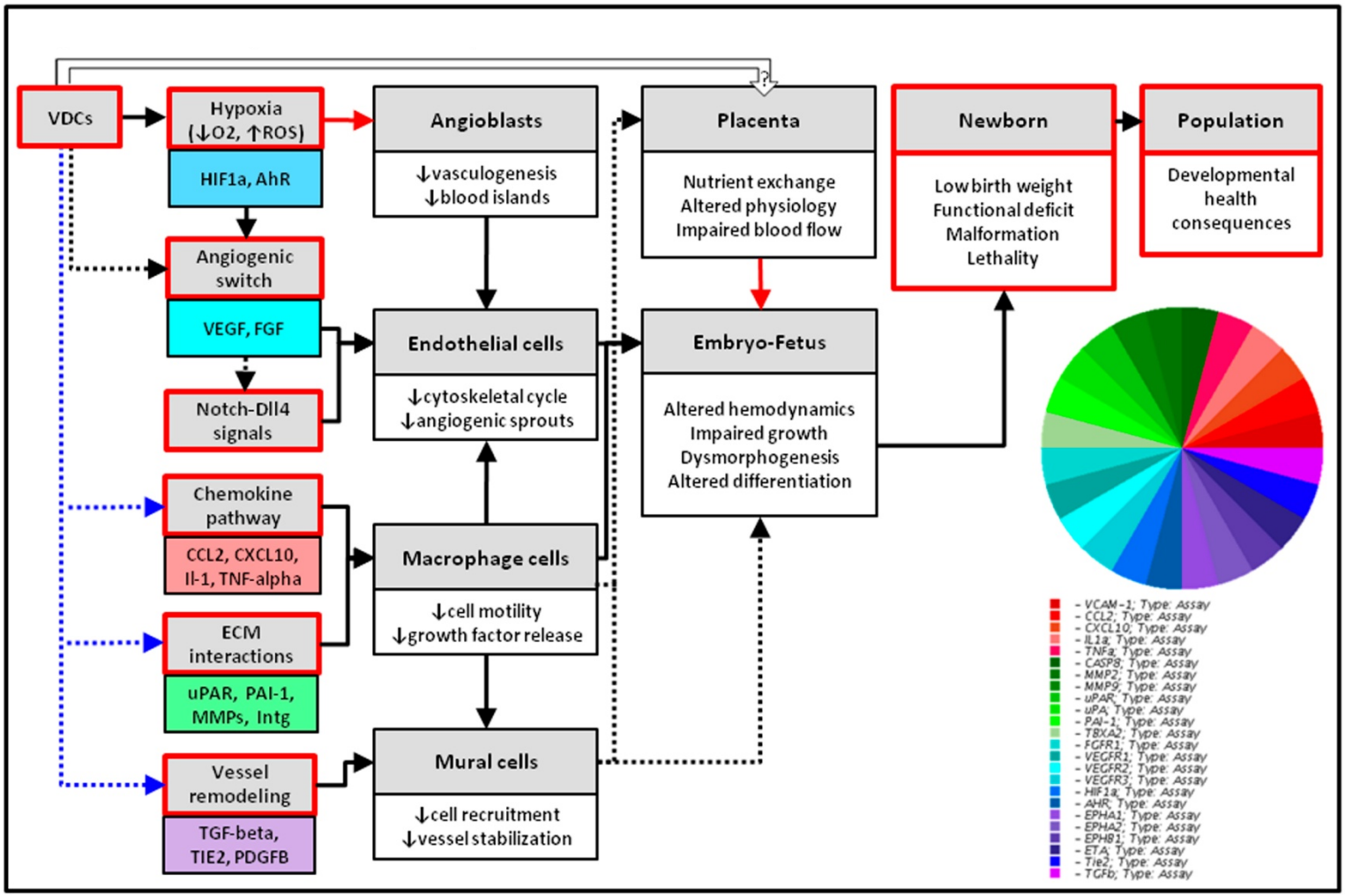
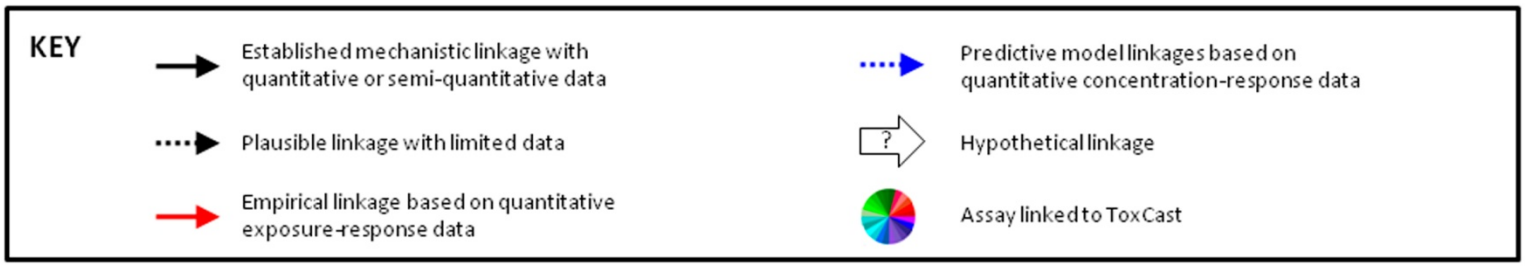
Identifying Chemical Contributors to Disease

- Identify Adverse Outcome Pathways (AOPs)
  - Link molecular initiating events to organism-level phenotypes
- Develop high-throughput *in vitro or in silico* assays
  - Test “Human Exposure Universe” chemicals in the assays
  - Up to 40,000 man-made chemicals in the environment
- Develop exposure models
  - Chemical use and distribution
- Prioritization and Risk Assessment

Adverse Outcome Pathway (AOP): Embryonic Vascular Disruption



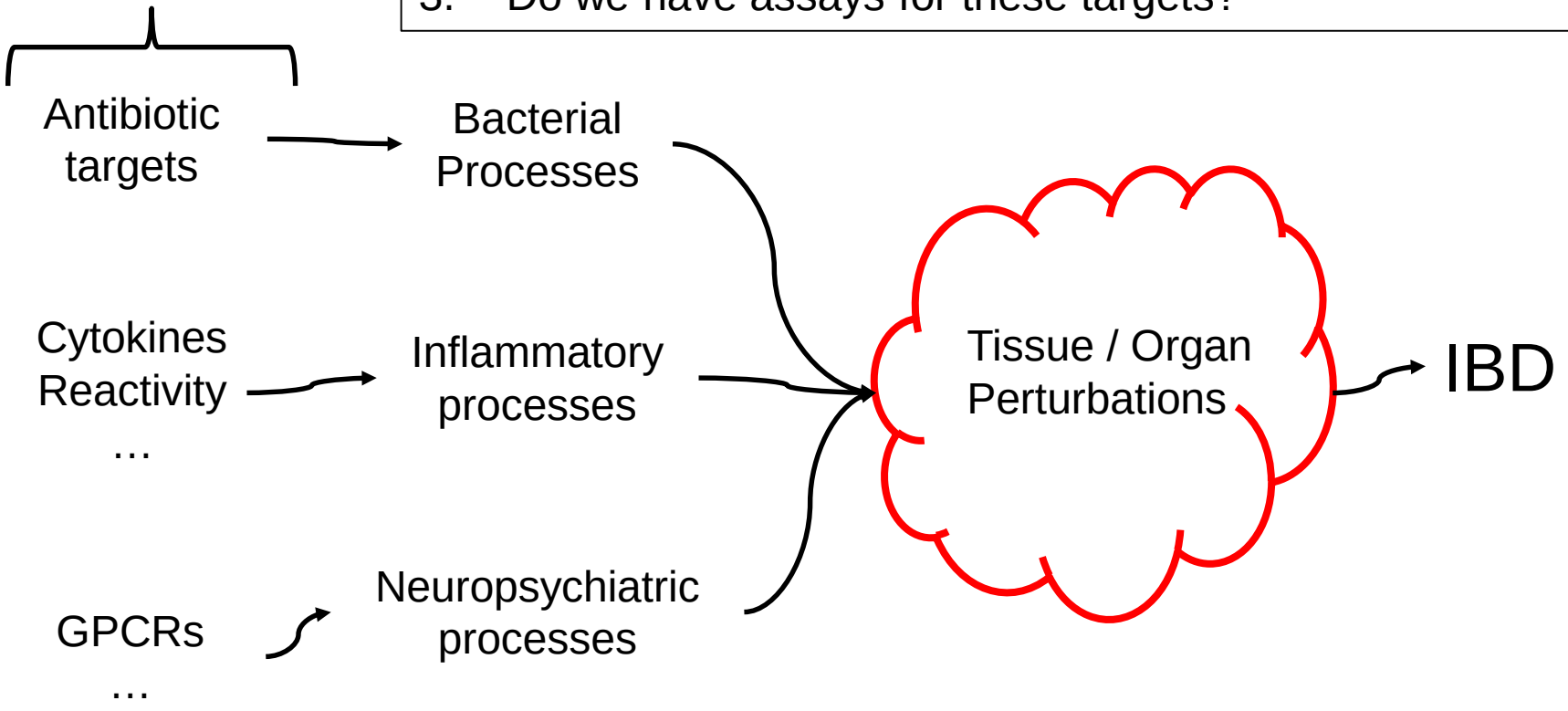


Knudsen and Kleinstreuer. Birth Def Res C. 2012

IBD AOP Starter …

Known Targets of Environmental Chemicals

Gaps:
1. What are the relevant processes?
2. What molecular initiating events trigger the processes?
3. Do we have assays for these targets?



Strategy Summary

1. Identify Pathways, Processes, Molecular Initiating Events (MIEs)
2. Develop High-throughput Assays
3. Screen Candidate Chemicals

Hazard

Measure Exposure or
Apply exposure models

- Use
- Distributions

Exposure