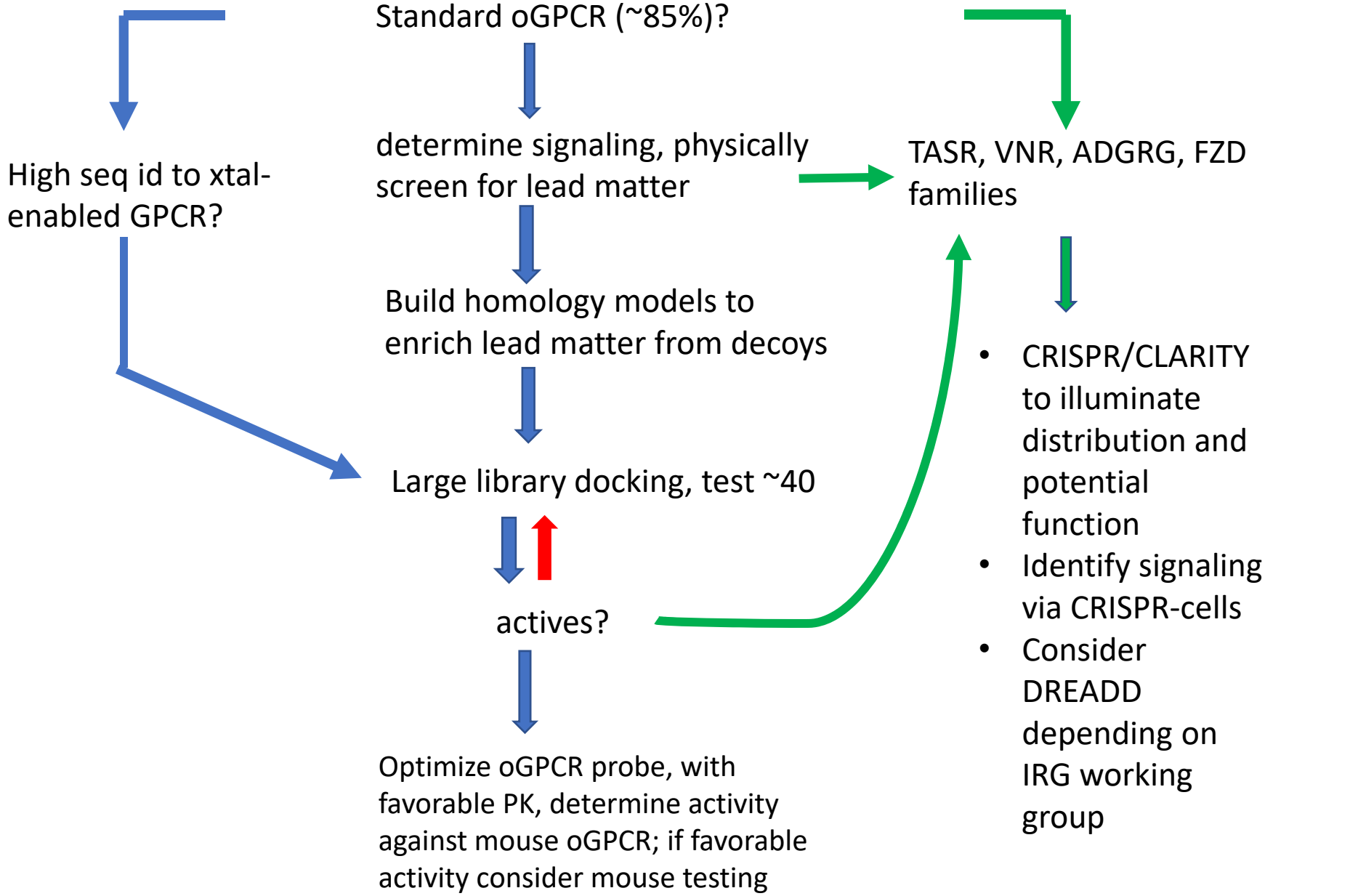
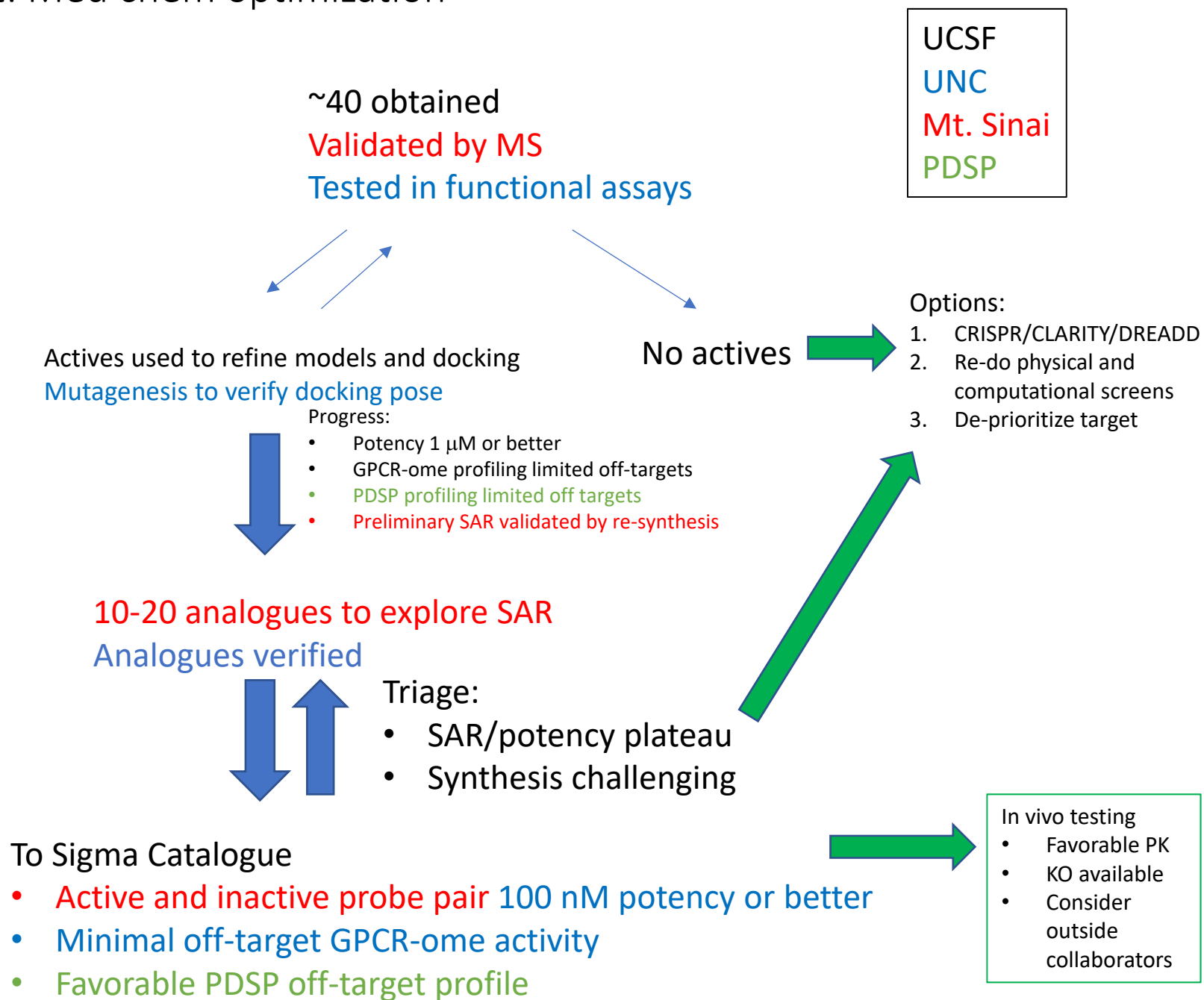


oGPCR decision tree



Flowchart: Med chem optimization oGPCRs



CRISPR-Clarity-DREADD

TASR, VNR, ADGRG, FZD families and oGPCRs
failed modeling

UNC (Roth lab, Genetics
and Pathology Cores

UCSF and KMC

IDG Working Group

Targets prioritized by IDG Working Group

CRISPR knock-in design:

- Epitope tag (FLAG, HA) to minimize expression
- IRES-Cre

Initial knock-in fails:

- Redesign targeting guide RNAs
- May iterate x 2 before de-prioritization of target

Targeting achieved

- F1 obtained (UNC Genetics Core)
- Bred to reporter line (Roth lab)
- Survey of tissue distribution (Roth lab + UNC pathology core)

Input from IDG-WG

- Which targets to prioritize for survey vs in-depth interrogation
- DREADD go/no-go

Further anatomical and functional characterization:

- Whole body, single-cell resolution via iDISCO/CLARITY (UNC-Cal Tech collaborators)
- Deposition of images (UCSF/KMC)
- DREADD-based activation of signaling to elucidate physiology
- Videos of physiology deposited (UCSF/KMC)