

Discovery Pathway Advisory Group (DPAG)

- DPAG will offer independent and impartial support, advice and assessment to early translational projects and funding applications. Its primary purpose is to enhance:
 - The implementation of on-going early translational studies;
 - The quality of applications for early translational funding to schemes such as the UoM/MRC Confidence in Concept;
 - The success of follow-on funding applications and commercial development after proof-of-concept has been obtained.



DPAG membership

- A virtual group that will allow us to readily identify individuals whose experience could help other academics working on drug, device or biomarker discovery facing activities and associated grant applications.
- Where appropriate this can also help us to utilise our wider networks, both within and outside of the University.
- When relevant projects come up Sam/Anu will contact specific individuals or the wider group to request peer review or advice.
- We can't promise to help... but we will try!
- January 2018 over 30 individuals identified and contacted, current membership stands at 24 from across FMBH and FSE.

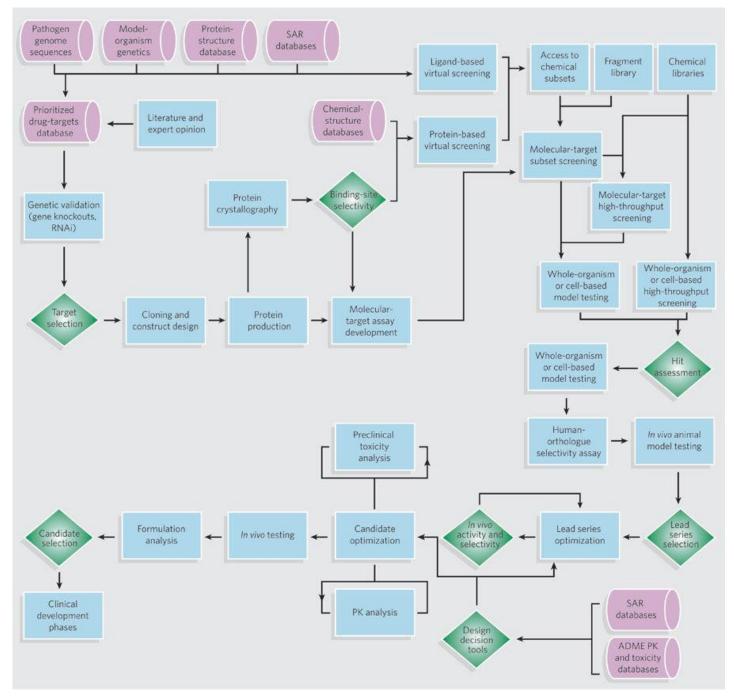
| Name | Area/Key Words |
|------------------|--|
| Sam Butterworth | Medicinal chemistry, tool/lead identification strategy, general advice |
| Anu Suokas | Strategic Funding team |
| Pip Peakman | MCRC |
| Rick Watson | IP |
| Cat Headley | Unmet need, development pathway market access |
| Elaine Bignell | Antifungals |
| Mike Bromley | Antifungals |
| Lydia Tabernero | Structural Biology |
| Jeremy Derrick | Structural Biology |
| Doug Kell | Systems biology |
| Sally Freeman | Medicinal chemistry |
| Richard Bryce | Computational chemistry |
| Kaye Williams | In vivo models and dosing/formulation |
| Alex Galetin | Pharmacy: Pharmacokinetics/ADME |
| Leon Aarons | PKPD modeling |
| Alan Dickson | Cell lines, construct issues, biopharmaceuticals |
| Sarah Cartmell | Medicines and Materials |
| Kevin O'Brien | Clinical trial design |
| Andy Vail | Clinical trial design |
| Mohammed Zubair | Regulatory key issues strategy |
| Matthew Krebs | Clinical trials |
| Tony Freemont | Biomarker discovery |
| Katherine Boylan | Biomarker discovery |
| Curtis Dobson | Devices |

| Name | Area/Key Words |
|------------------|--|
| Sam Butterworth | Medicinal chemistry, tool/lead identification strategy, general advice |
| A 6 1 | |
| Anu Suokas | Strategic Funding team |
| Pip Peakman | MCRC |
| Rick Watson | IP |
| Cat Headley | Unmet need, development pathway market access |
| Elaine Bignell | Antifungals |
| Mike Bromley | Antifungals |
| Lydia Tabernero | Structural Biology |
| Jeremy Derrick | Structural Biology |
| Doug Kell | Systems biology |
| Sally Freeman | Medicinal chemistry |
| Richard Bryce | Computational chemistry |
| Kaye Williams | In vivo models and dosing/formulation |
| Alex Galetin | Pharmacy: Pharmacokinetics/ADME |
| Leon Aarons | PKPD modeling |
| Alan Dickson | Cell lines, construct issues, biopharmaceuticals |
| Sarah Cartmell | Medicines and Materials |
| Kevin O'Brien | Clinical trial design |
| Andy Vail | Clinical trial design |
| Mohammed Zubair | Regulatory key issues strategy |
| Matthew Krebs | Clinical trials |
| Tony Freemont | Biomarker discovery |
| Katherine Boylan | Biomarker discovery |
| | |
| Curtis Dobson | Devices |

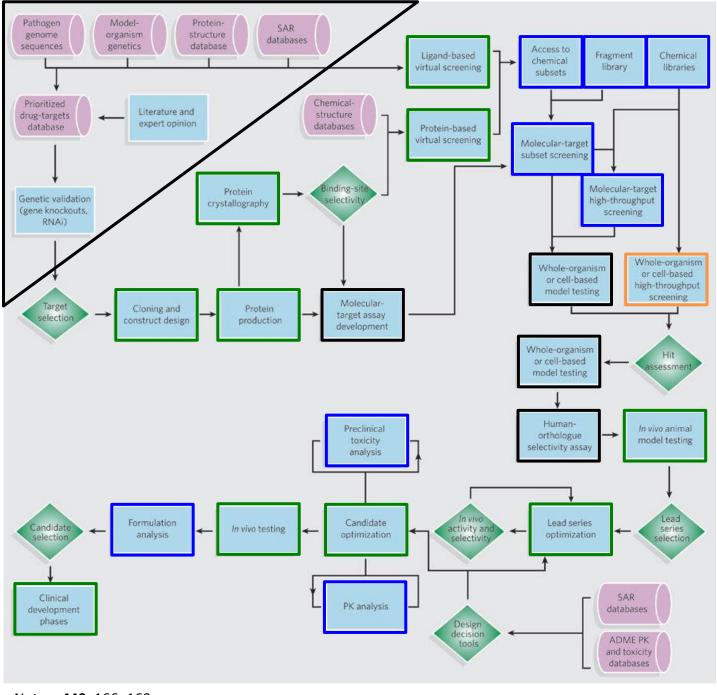
| Therapeutics |
|----------------|
| Diagnostics |
| Devices |
| Digital health |
| Mixed? |

Small Molecule 4D Map A. Basic science research & Biomarker dev't B. Target Pharmac logy & biomarker develo Identification target identification program (B) Development (C) Pharmacology 8 Assay Biomedical Disease target engagem HTS assay Therapeutic Development generation Pathophysiology informatics targets Biomarker dev't program Data mining New indication/ Cell lines Animal Molecular libraries informatics Repurposing (G) models pathway Prognostic & Data predictive narkei biomarker Genotypes 4 Phenotypes **HTS System** Biorepositories Qualification Misses Hits Qualified Researcher/ Registries/EMRs Biospecimens Companion investigators and Surre investigator endr oint diagnostics Unapproved compounds study staff (NCE/NME) IRB review Natural history & Clinical Clinical trial plan Cohorts epi. studies IRB approval & preparati D. Lead optimization, Contractual & candidate selection, Clinical trial IND (F) legal agreements ND-enabling studies planning & Population-specific Lead preparation scale-up for events from Study sponsor Recruitment severity measures compounds manufacturing existing therapy Informed consent In silico modeling Lead Identification of target population compliance strategy optimization Clinical program Therapeutic and Participant or In vitro functional Clinical & trial design clinical endpoints & safety screening health subject chemistry Cohorts enrollment FDA review Natural Process Non-GMP supply Preapproval Pathophys optimization history & IND chemistry & early CMC clinical trials epi. studies iology (E) (A) Phase I Translational PK/PD, Reporting, meetings, Candidate compounds pharmacology safety, dose amendments Non-GLP studies Patient Clinical Investigative Phase II safety, POC, dose vitro/in vivo safety NDA pharmacology & toxicology Standard of care FDA review -Phase III Safety Effectiveness and POC safety, efficacy Complete Response Marketing Access to Letter (Rejection) Reevaluate or therapies discontinue Predicted therapeutic dose/exposure F. Regulatory E. Clinical research Short list for preclinical candidates & development review Postapproval Incorporation into Data Collection clinical practice Pharmaco. Early cGMP manufacturing epidemiological Pragmatic safety Reanalysis of Spontaneous observational & effectiveness GLP preclinical studies premarket data studies trials Insurance coverage & reimbursement Pharmacokinetics Pharmacology Toxicology Extend to related drugs knowledge Pricing New indication/ Long-term toxicology; Additional studies repurposing reproductive toxicology; H. Medical Changed drug carcinogenesis; etc. FDA review landscape Hypothesis Late CMC (e.g., Postmarketing Sustained product generation (A) commitments/requirements G. Postmarketing

Even this is oversimplified relative to the complexities of an actual project...



Nature 449, 166-169



Project specific

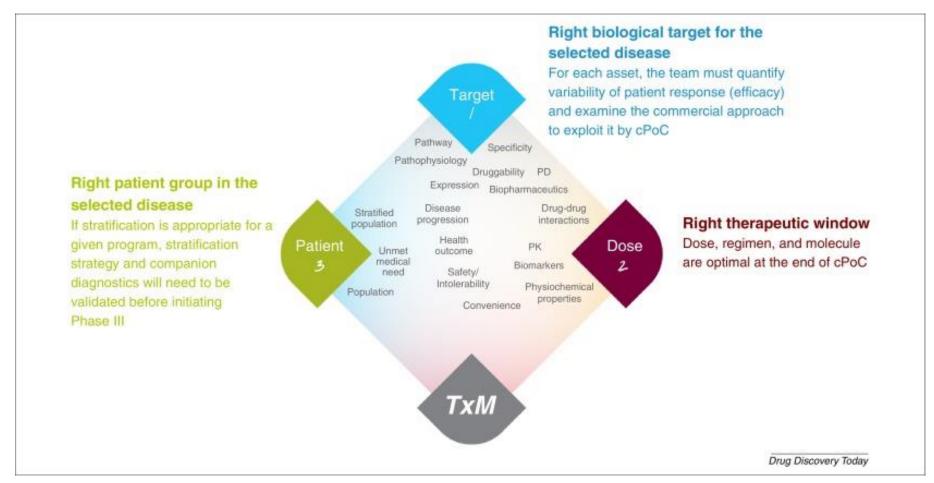
Knowhow and capability

Less covered?

Knowhow but no capability

There is more to successful translational applications than just have the right data and plan...

e.g. Line of Sight, TPPs, clinical vs statistical significance.



Drug Discovery Today 2016, 21/3, p517-526