Academic drug discovery within the United Kingdom: a reassessment

Emma Shanks, Robin Ketteler and Daniel Ebner

In 2014, Tralau-Stewart *et al.* published an overview of academic drug discovery efforts in the United Kingdom based on a survey they conducted (UK academic drug discovery, *Nature Rev. Drug Discov.* 13, 15–16 (2014))¹. They observed that academic screening within the United Kingdom is comparable to that in the United States (discussed in REF. 2) with regard to primary therapeutic focus (with cancer, infectious disease and cardiovascular disease constituting the most highly prioritized therapeutic indications) and areas of unmet medical need. Parallels were also drawn between the motivational drivers and annual operating costs of screening in both countries. However, regarding infrastructure, it was reported that most drug discovery programmes in academic screening groups (ASGs) in the United Kingdom were conducted in a traditional research group (that is, a team of postdoctoral researchers, Ph.D. students and technicians led by a single principal investigator), with only 13% of groups operating in centres dedicated to drug discovery. The most surprising finding was that “access to high-throughput screening (HTS) facilities and associated compound libraries were not reported by any UK group” (REF. 1). Tralau-Stewart *et al.* clearly stated that the responses provided a “snapshot” of academic research at the time of the survey (2013) and not a comprehensive analysis, as some groups may not have received or responded to the survey¹. However, it seems to us that the presence of centre-led ASGs and industry-standard drug discovery programmes conducted within an academic environment in the United Kingdom was substantially understated by the survey results. Therefore, we conducted another investigation of the academic drug discovery landscape in the United Kingdom by identifying academic drug discovery units and facilities and analysing their characteristics, which we discuss here.

UK drug discovery facilities

We identified 24 dedicated drug discovery facilities in the United Kingdom (TABLE 1; see also the [UK Drug Discovery Consortium](#) website in Further information). These facilities have a range of operational

frameworks: some are academic facilities operated by universities with several sources of funding; several are operated by charitable organizations; and others are industrial facilities sited on or near to academic campuses. The common theme linking these groups is that they are all open-access drug discovery facilities that are accessible by UK-wide academic groups, and each facility employs some personnel from academia, thereby strengthening links to the UK academic community. These groups may therefore be better referred to collectively as academic and not-for-profit screening groups; hereon, we refer to them as ASGs.

The scale of the undertaking and resourcing of these groups varies according to the objectives of each facility. Some groups provide dedicated support for distinct aspects of the drug discovery pipeline (for example, target discovery or identification of chemical starting points for nominated disease indications) and are resourced with the relevant expertise and technical knowledge. At least six ASGs conduct industry-standard drug discovery, resourced largely by professionals with substantial industrial experience, and they incorporate extensive in-house medicinal chemistry expertise and drug metabolism and pharmacokinetics (DMPK) resources.

All of the identified groups reported that they had conducted multiple high-throughput screens (HTSs) in the past year (TABLE 1). They actively pursue primary screen hits for further validation or drug development, and they regularly publish their results in peer-reviewed scientific journals. Additionally, we found that all of the groups use industry-standard liquid handling and/or readout instruments and have research staff dedicated to each step of the drug discovery pipeline (for example, compound management, assay development, screening and data analysis) suggesting that their facilities are well equipped with both instrumentation and personnel. These facilities represent a major investment in UK drug discovery research. The similarity in facility numbers between the United Kingdom and the United States highlights a clear commitment in the United Kingdom to provide the infrastructure necessary to support academic screening.

Funding and collaboration

Currently, the majority of funding for the main UK-based ASGs is provided by the UK government, with considerable support coming from universities, UK-based and international charitable organizations (for example, Cancer Research UK (CRUK), which supports programmes at 5 of the 23 facilities), and the UK Medical Research Council. In addition to government and charitable funding streams, we have recently experienced a paradigm shift in the perception of academic screening by the industrial sector. Pharmaceutical companies now recognize the potential of academic alliances and several have entered into partnerships with UK-based ASGs. Collaborative efforts to address a broad range of disease areas are underway (TABLE 1), through the provision of well-characterized compound collections (GlaxoSmithKline (GSK) and Pfizer) and engaging closely with academic partners to enhance their own drug discovery capacity. Notable examples include AstraZeneca's Open Innovation Initiative, GSK's Centre for Therapeutic Target Validation (CTTV) and the Eisai–University College London (UCL) collaborative drug discovery alliance. These partnerships are evidence that the UK academic screening community is held in high esteem by global pharmaceutical companies.

Screening platforms and technologies

The approaches used across ASGs are multidisciplinary yet complementary: the identification and de-risking of potential targets using high-throughput functional genomics helps to bridge the gap between the academic research and drug discovery disciplines^{3,4}. Platforms such as RNA-mediated interference (RNAi) screening can support target identification and concurrently provide novel biological insights. Moreover, dedicated efforts to unearth novel chemical starting points for drug discovery are increasing, supplemented by committed medicinal and/or computational chemistry for the development of lead compounds. The repurposing of existing therapeutics is increasingly complementing the more traditional drug discovery workflow as more groups begin to use screening to explore the potential applications of existing drugs for alternative indications⁵.

ASGs have also been a driving force behind the development and implementation of high-content imaging and analysis in drug discovery. We found that all of the UK-based ASGs that are engaged in cell-based phenotypic screening use state-of-the-art high-content imagers, and most use multiple instruments. Other platforms typically perceived to be restricted to use only by pharmaceutical

Table 1 | Drug discovery facilities in the United Kingdom*

Facility	Host institution	Main disease indications	Funding sources	Staff	Platforms	Technologies	No. of screens per year	Medicinal chemistry follow-up
Dundee Drug Discovery Unit[†]	University of Dundee	Diseases of the developing world and innovative targets and pathways	UK government, charities and industry	>70	Biophysical, biochemical and cellular assays	Multiple	NA	Yes
National Phenotypic Screening Centre	University of Dundee, University of Oxford and University of Edinburgh	All diseases, with human prioritized over non-human	UK government, charities and industry	~25	Small molecules, 3D, tissue, patient cells, iPS cells and genome engineering	HCI, MPA, label-free and HT flow cytometry	10–15	Yes
European Screening Centre Newhouse and European Lead Factory	Multiple sites across the United Kingdom (including Dundee and Lanarkshire) and Europe	All human diseases	Innovative Medicines Initiative and in-kind contributions from EFPIA participants	50	Small molecules (326,000 [§]), biophysical and biochemical assays	Ultra-HTS plate-reader, SPR and label-free	30	Yes
Edinburgh Cancer Discovery Unit	Edinburgh Cancer Research Centre, University of Edinburgh	Oncology	Industry alliances, MRC and University of Edinburgh	14	Small molecules and chemical library synthesis	HCI, MPA, image informatics, reverse phase protein array and dual ligand	12	Yes
Beatson Institute RNAi Screening Facility	CRUK Beatson Institute, University of Glasgow	Oncology	CRUK	5	Genome-wide human and mouse RNAi and drug repurposing	HCI, MPA and HTS plate reader	8	No
Beatson Institute Drug Discovery Unit	CRUK Beatson Institute, University of Glasgow	Oncology	CRUK	30	Fragments	NMR and SPR	1–5	Yes
Scottish Bioscreening Facility	Institute of Infection, Immunity and Inflammation, University of Glasgow	Neglected diseases and parasitology	Wellcome Trust and SULSA	3	Small molecules and RNAi	HCI and HTS plate reader	6	Yes
Queen's University Belfast Drug Discovery Group	Queen's University, Belfast	Oncology	Almac, Queen's University and Invest Northern Ireland	20	Fragments, CADD and virtual screening	SPR, thermophoresis, Schrodinger, MOE, HCI and MPA	3	Yes
Medicinal Chemistry and Chemical Biology Technology Group	University of Leeds	All human diseases	University of Leeds, UK government, charities and industry	5	Small molecules (50,000), drug repurposing, fragments and virtual screening	Biochemical, phenotypic and biophysical	5–10	Yes
Bioscreening Technology Group	University of Leeds	All human diseases	University of Leeds, UK government, charities and European Commission	2	Genome-wide human and mouse RNAi, miRNA inhibitors and mimics, small-molecule screening and drug repurposing	HCI, MPA and HTS plate reader	5–8	Yes
Adhiron Screening Facility	University of Leeds	All human diseases	University of Leeds, UK government, charities and industry	19	Biologics	Phage display, biochemical and biophysical	150	Yes

Table 1 (cont.) | **Drug discovery facilities in the United Kingdom***

Facility	Host institution	Main disease indications	Funding sources	Staff	Platforms	Technologies	No. of screens per year	Medicinal chemistry follow-up
Manchester Institute Drug Discovery Unit	CRUK Manchester Institute, University of Manchester	Oncology	CRUK	5	Small molecules and drug repurposing	HCI	5–10	Yes
Sheffield RNAi Screening Facility	University of Sheffield	Oncology, Parkinson disease and myeloproliferative neoplasms	Wellcome Trust, Yorkshire Cancer Research and University of Sheffield	2	Genome-wide drosophila RNAi, human siRNA and small molecules	HCI, MPA and HTS plate reader	16	No
SITraN Drug Discovery Suite	University of Sheffield	Motor neuron disease and Parkinson disease	Wellcome Trust, MRCT, MND and Parkinson's UK	6	Small molecules	HCI, MPA, HTS plate reader and metabolic outputs	2	No
Zebrafish Small Molecule Screening Unit	University of Sheffield	Zebrafish models of disease, including epilepsy, inflammation, infection, hypoxia and ototoxicity	MRC, BBSRC, charities and industry	1	Small molecules	HCI, MPA, HTS plate reader and microscopy	5–10	Yes
Drug Discovery Priority Group	University of Nottingham	All human diseases	Charities, industry and the European Union	2	Small molecules	HCI and HTS plate reader	2–4	Yes
Birmingham Drug Discovery Facility	University of Birmingham	Infectious diseases (tuberculosis, and <i>Salmonella enterica</i> and <i>Staphylococcus aureus</i> infection), leukaemia, lymphoma and HBV	MRC, Wellcome Trust and ERC	3	Small molecules	HTS plate reader	5	Yes
CRT Discovery Laboratory	Babraham Research Campus, Cambridge	Oncology	Industry alliances, CRT and CRUK	74	Small molecules (>100,000), fragments and RNAi	HCI, MPA, HTS plate reader, MSD technology, SPR, ITC and crystallography	6	Yes
Target Discovery Institute	University of Oxford	Oncology, cardiovascular and neuro-degeneration	UK government, University of Oxford, UK charities, industry and SRFs	>50	Small molecules (50,000), drug repurposing, fragments and RNAi	HCI, HTS plate reader, RT-PCR and HTFACS	20	Yes
CRUK Cancer Therapeutics Unit	The Institute of Cancer Research, London	Oncology	CRUK, ICR, Wellcome Trust and industrial collaborators	143	Small molecules (210,000), fragments (2,000) and siRNA	HCI, HTS plate reader, mobility shift assays, SPR, ITC, DSF and crystallography	3	Yes
High-throughput Screening Facility	Crick Institute	Oncology	CRUK	4	Genome-wide RNAi, small molecules (4,000) and fragments	HCI, MPA, HTS plate reader, thermal melt and FACS	20–30	No
Laboratory for Molecular Cell Biology	University College London	Neurodegeneration, oncology, HIV, cell biology	MRC	4	RNAi, cDNA, small molecules, CRISPR	HCI, MPA, HTS plate reader	15–20	Yes
MRCT	MRC, London	All including oncology, fibrosis, neurodegeneration, inflammation, anti-infectives, pain, autoimmune disease, Cushing disease	Self-funded through income from translational activities		Small molecules (>250,000), phage and antibodies	HCI, MPA, HTS plate reader, label free, SPR, ITC, thermal shift	8–10	Yes

Table 1 (cont.) | **Drug discovery facilities in the United Kingdom***

Facility	Host institution	Main disease indications	Funding sources	Staff	Platforms	Technologies	No. of screens per year	Medicinal chemistry follow-up
Translational Drug Discovery Group	University of Sussex	Oncology, neuroscience	Wellcome Trust, CRUK	18	Structure-based drug discovery	Biophysical, crystallography, virtual screening, high-throughput electrophysiology	4	Yes

ARUK, Alzheimer's Research UK; BBSRC, Biotechnology and Biological Sciences Research Council; BHF, British Heart Foundation; CADD, combined annotation dependent depletion; CRISPR, clustered regularly interspaced short palindromic repeats; CRT, Cancer Research Technology; CRUK, Cancer Research UK; DSF, differential scanning fluorimetry; EFPIA, European Federation of Pharmaceutical Industries and Associations; ERC, European Research Council; FACS, fluorescence-activated cell sorting; HBV, hepatitis B virus; HCI, high-content imaging; HT, high-throughput; HTS, HT screening; iPS cells, induced pluripotent stem cells; ICR, Institute of Cancer Research; ITC, isothermal titration calorimetry; miRNA, microRNA; MND, Motor Neurone Disease Association; MOE, multivariate optical element; MPA, multiparametric phenotypic analysis; MRC, Medical Research Council; MRCT, MRC Technology; MSD, mesoscale delivery; NA, not applicable (information unavailable); NMR, nuclear magnetic resonance; RNAi, RNA-mediated interference; RT-PCR, real-time PCR; siRNA, short interfering RNA; SITraN, Sheffield Institute for Translational Neuroscience; SPR, surface plasmon resonance; SRFs, small research facilities; SULSA, Scottish Universities Life Science Alliance. *The authors apologize to any academic screening group (ASG) they may have overlooked. ASGs are ordered from north to south within the UK. [†]Data collated from facility website. [‡]To be expanded to 500,000 compounds by 2017.

companies, such as acoustic dispensing, are now well embedded in ASGs, with a total of 19 Echo systems (Labcyte) at 14 ASG sites.

Tralau-Stewart *et al.* also reported an apparent lack of uptake of HTS (defined as screening collections of >100,000 compounds) in UK-based ASGs. However, at the time of their survey, both the CRUK Cancer Therapeutics Unit at the Institute of Cancer Research and the Cancer Research Technology (CRT) Discovery Laboratory were regularly screening >100,000 compounds. Along with the Medical Research Council Technology (MRCT) and Dundee Drug Discovery Unit, these centres are capable of large-scale screening, although it is still not commonplace in ASGs. Given the limitations in funding, this will probably remain the case, as it is, arguably, unnecessary to duplicate such efforts. Typically, ASGs use either high-diversity libraries of 10,000–50,000 compounds or smaller, more focused compound sets. Notably, there has recently been a dramatic change in the perception of the necessity of screening very large libraries of compounds to identify the most appropriate starting points for innovative drug discovery, catalysed by understanding of the substantial contribution of phenotypic approaches in identifying first-in-class drugs⁶. The focus has shifted to screening fewer, more discrete, well-designed and diverse compound libraries. When coupled with advanced computational approaches to explore chemical space *in silico*⁷, it becomes evident that the size of screening collections is not necessarily the most crucial criterion for success in primary HTS.

Discussion

Screening within an academic environment forms an integral part of drug discovery initiatives within the United Kingdom, and efforts in this area have undergone

dramatic expansion over the past 10 years. Furthermore, the strategic alliance between academia, the UK government and the pharmaceutical industry is exemplified by the £8 million investment into the National Phenotypic Screening Centre (NPSC, 2014; sourced principally from the Scottish Government via the Scottish Funding Council with both academia and industry supporting running costs) and by the establishment of the European Screening Centre (which supports researchers and small- and medium-sized enterprises in screening ~300,000 compounds, collectively contributed by 7 pharmaceutical companies). While the sources and timescales of funding continue to evolve, the level of investment in the infrastructure and research of UK-based ASGs may represent an emerging cultural shift in the recognition of the value of academic drug discovery efforts.

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Competing interests statement

The authors declare no competing interests.

FURTHER INFORMATION

Adhiron Screening Facility: http://www.fbs.leeds.ac.uk/staff/profile.php?tag=Tomlinson_D

Beatson Institute Drug Discovery Unit: <http://www.beatson.gla.ac.uk/drug-discovery/drug-discovery.html>

Beatson Institute RNAi Screening Facility: <http://www.beatson.gla.ac.uk/advanced-technologies/emma-shanks-rnai-screening.html>

Birmingham Drug Discovery Facility:

<http://www.birmingham.ac.uk/facilities/bddf/index.aspx>

Bioscreening Technology Group: <http://medhealth.leeds.ac.uk/info/360/facilities/909/bioscreening-technology-group>

CRT Discovery Laboratory:

<http://www.cancertechnology.co.uk/>

CRUK Cancer Therapeutics Unit: <http://www.icrac.uk/our-research/our-research-centres/cancer-research-uk-cancer-therapeutics-unit>

Drug Discovery Priority Group: <http://nottingham.ac.uk/research/priorities/drugdiscovery/index.aspx>

Dundee Drug Discovery Unit:

<http://www.drugdiscovery.dundee.ac.uk/home>

Edinburgh Cancer Discovery Unit:

<http://www.ecrc.ed.ac.uk/discovery-unit/overview.html>

European Lead Factory: <http://www.europeanleadfactory.eu>

European Screening Centre Newhouse:

<http://www.lifesci.dundee.ac.uk/research/esc>

High-throughput Screening Facility: <http://www.crick.ac.uk/Laboratory-for-Molecular-Cell-Biology>

Manchester Institute Drug Discovery Unit:

<http://www.cruk.manchester.ac.uk/Research/CRUK-MI-Groups/Drug-Discovery/Home>

Medicinal Chemistry and Chemical Biology Technology

Group: <http://medhealth.leeds.ac.uk/info/1930/medicinal-chemistry-and-chemical-biology-technology-group>

MRCT: <http://www.mrcrcttechnology.org/about-us/>

Queen's University Belfast Drug Discovery group:

<http://www.qub.ac.uk/research-centres/CentreforCancerResearch/CellBiology/Research/EnablingTechnologies/DrugDiscovery>

National Phenotypic Screening Centre:

<http://www.sulsa.ac.uk/research-facilities/uk-national-phenotypic-screening-centre>

Scottish Bioscreening Facility: <http://www.gla.ac.uk/researchinstitutes/iii/facilities/imaging/sbfglasgow/>

Sheffield RNAi Screening Facility:

<http://www.rnai.group.shef.ac.uk>

SITraN Drug Discovery Suite: <http://sitran.dept.shef.ac.uk/>

Target Discovery Institute: <http://www.tdi.ox.ac.uk/home>

Translational Discovery Group:

<http://www.sussex.ac.uk/lifesci/drugdiscovery/>

UK Drug Discovery Consortium: <http://www.ukddc.org/>

Zebrafish Small Molecule Screening Unit:

<http://www.bateson.group.shef.ac.uk/research/facilities/sheffield-zebrafish-screening-facility/>

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