Creating (and managing) consortia – 3 case studies

Some things to keep in mind through the case studies

It is critical to understand incentives, so you can find a path to align them

1. When asked, industry research managers rank “ability to secure IP” low among the reasons to work with universities

2. Universities are rather homogeneous, but there is no such thing as “industry”

3. In general, national/state funders do not fund science as a public good, but to promote national interests, and often national economic interests

Scenarios most appropriate for consortia

1. Solving the problem requires skill sets from multiple sectors
2. Problem can be decomposed into *quantifiable* units
3. Problem transcends corporate, institutional or national interests

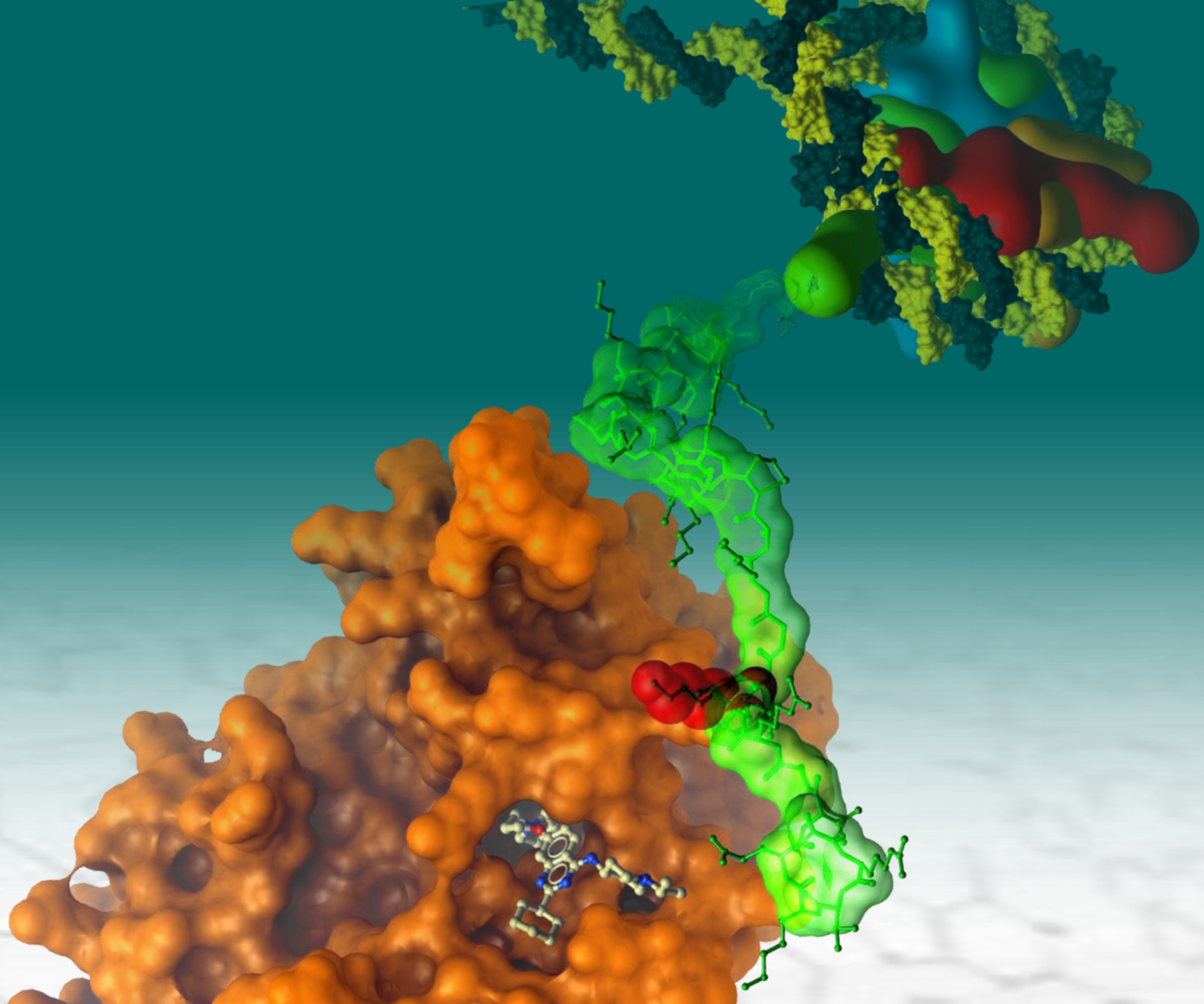
What I believe leads to successful consortia

1. Every participants can see a win

2. Leadership not linked to an institution

3. *Very* clear mission

SGC



www.thesgc.org

SGC IS A MISSION-DRIVEN, OPEN SCIENCE RESEARCH ORGANIZATION

- **INTERNATIONAL PUBLIC-PRIVATE PARTNERSHIP (PPP)** WITH A MISSION TO ACCELERATE THE DISCOVERY OF NEW MEDICINES THROUGH PRECOMPETITIVE, OPEN SCIENCE
- **SGC HEAD OFFICE IS IN CANADA,** INCORPORATED IN THE UK, FOUNDED IN 2003
- **SGC FUNDS A NETWORK OF SCIENTISTS IN 6 UNIVERSITIES IN 5 COUNTRIES**
- **CONTINUOUSLY FUNDED FOR 19 YEARS BY 13 PHARMACEUTICAL COMPANIES** AND SEVERAL OF THE WORLD'S LARGEST FOUNDATIONS AND GOVERNMENT AGENCIES
- **SGC CO-AUTHORS ~125 PEER-REVIEWED PAPERS EACH YEAR, ~25 WITH INDUSTRY CO-AUTHORS**

The problem in 1999

- The Human Genome Project revealed thousands of new proteins
- Their 3D structures are *enabling* to drug discovery
- Academics were avoiding working on human proteins in lieu of simpler bacterial proteins
- Biotechs and universities were jumping in and patenting human protein structures, and there was concern about a patent thicket ands FTO

The Structural Genomics Consortium concept

- Pharma (GSK, AZ and Pfizer) and Wellcome had the idea to create a charity to solve 3D structures and place the results in the public domain (no patents), creating ”freedom to operate”

- I was recruited and formed the SGC as a two-site research operation at Toronto (CSO, Cheryl Arrowsmith) and Oxford (CSO, Michael Sundström)

- Initial funding was ~$100M for 4 years (90% public and charitable) – only industrial partner that committed was GSK

The SGC was set clear goals

- In 2003, we were given quantitative goals of 350 structures in 3 years
  - Quality criteria were pre-established and clear
  - Target List was pre-established
  - Starting in 2004, we determined 455 structures
- In 2007, we were given new goal of 650 structures in 4 years
  - Same level of funding, but two new pharma joined (Novartis and Merck)
  - We determined 692 structures
- At peak structural output, we accounted for >20% of world's output

IMPACT OF SGC PROTEIN STRUCTURES TODAY

RCSB PDB PROTEIN DATA BANK

4,000+

DEPOSITED STRUCTURES

addgene

4,100+

PLASMIDS DISTRIBUTED

SGC www.theSGC.org

1,500+

DETAILED PURIFICATION PROTOCOLS

PubMed.gov

1,100+

PEER REVIEWED PUBLICATIONS OF STRUCTURES

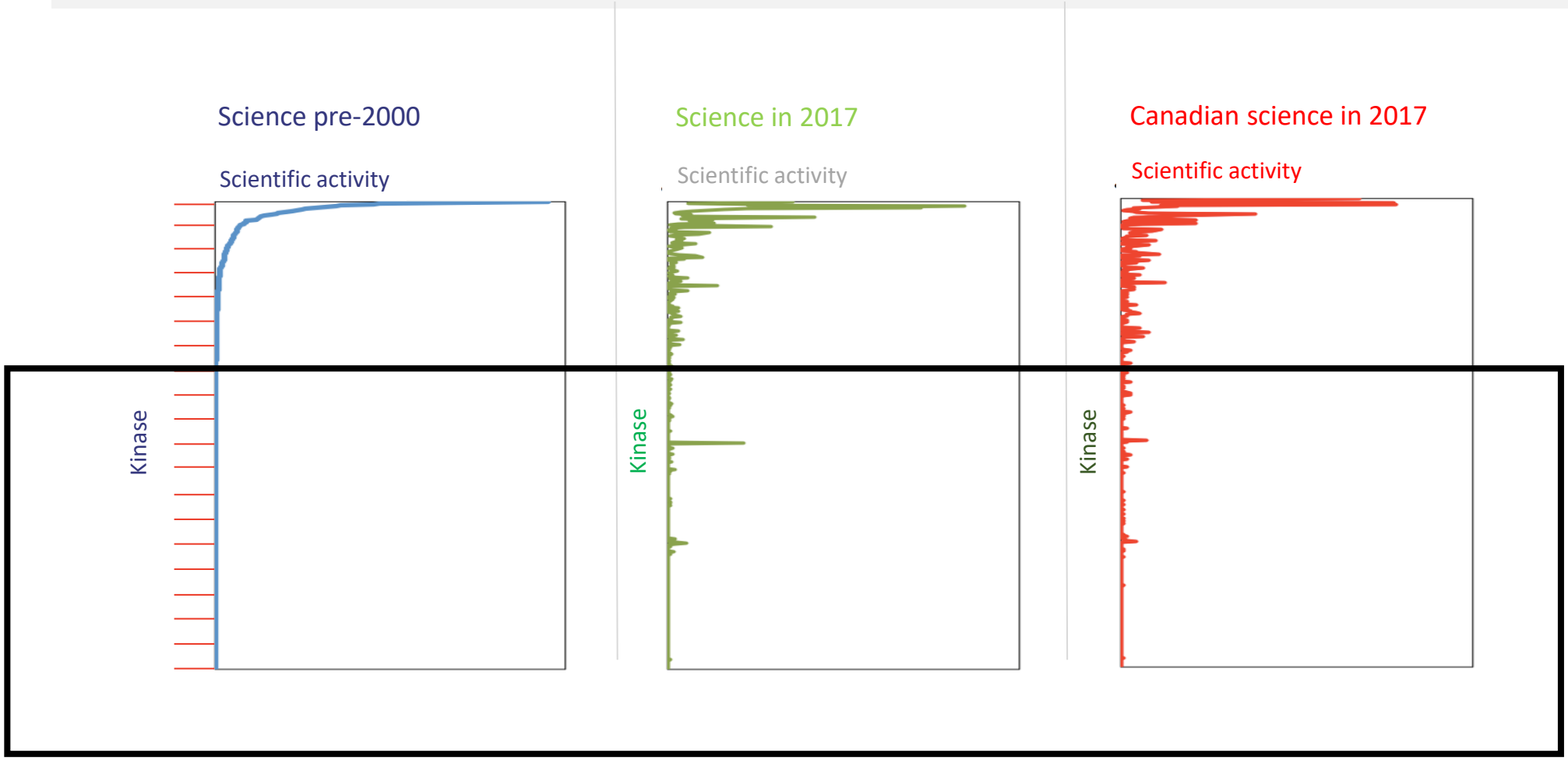
Emerging scenario in 2009

- Structural biology was becoming more routine

- We wanted to take learnings and apply them to arguably the biggest problem in biomedicine – determining the functions for all human proteins

Why is there need for a consortium to study human proteins?

Academia resists change and most of us are redundant



COMMENT

Too many roads not taken

Most protein research focuses on those known before the human genome was mapped. Work on the slew discovered since, urge **Aled M. Edwards** and his colleagues.

Every disease has same feature

Parkinson's

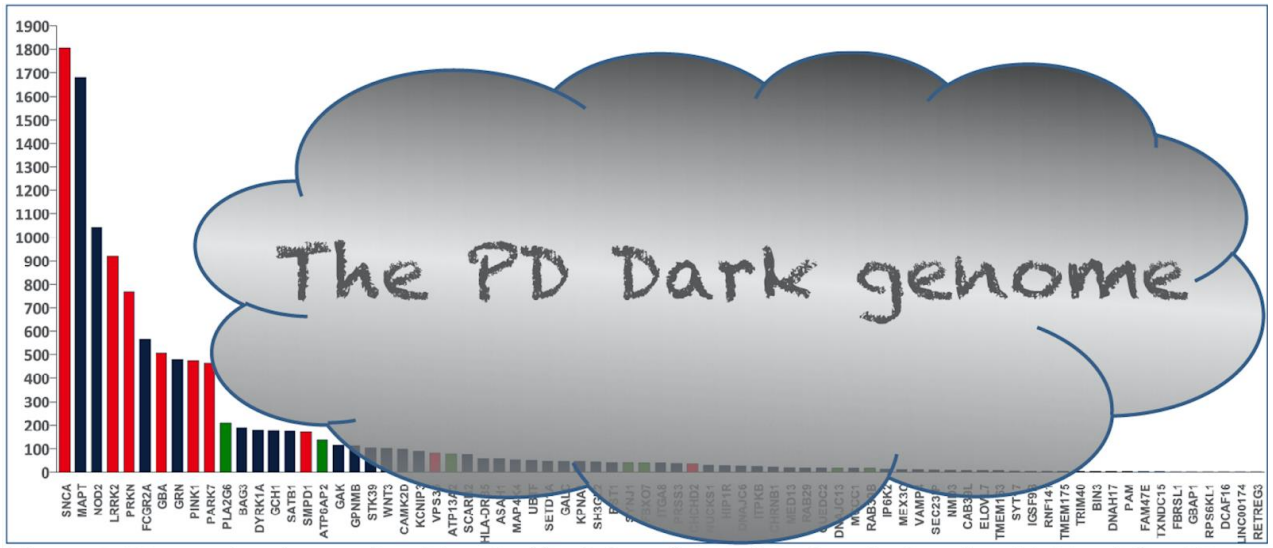
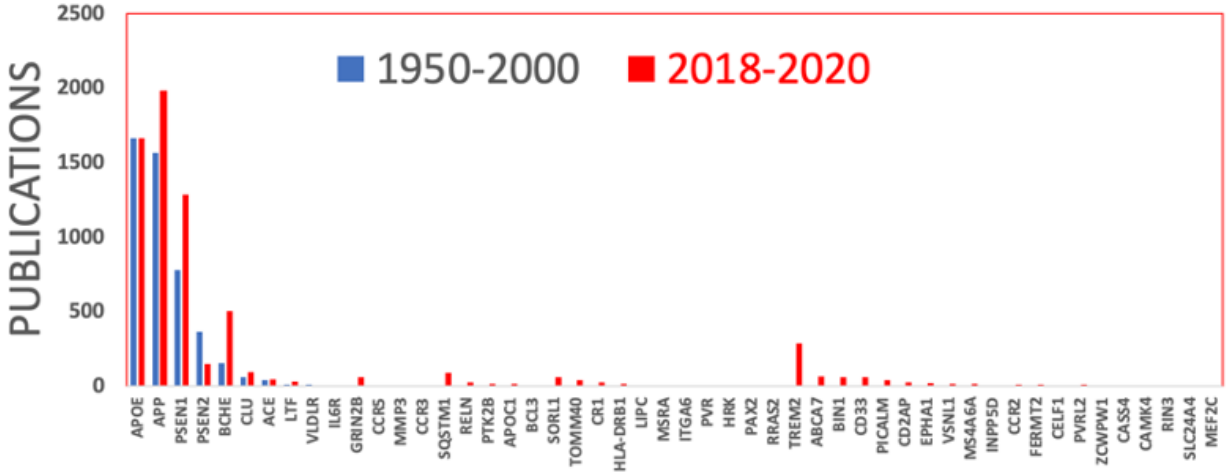


Figure 1: PD-associated genes (x axis) ranked by Pubmed gene function citations (y axis). Mendelian PD genes (red), genes associated with PD-like syndromes (green) and GWAS PD risk loci (dark blue).

Alzheimer's



SGC Chemical Probe Project (2008–

There is strong evidence (Edwards et al, Nature 2011) that the community will start to study a new proteins if they have open access to a high quality chemical probe

Problem: The skills to generate probes are in Industry

Solution: Create an open science environment to collaborate

Pre-competitive (no IP)

Industry | SGC | Academia

- Early lead compound series
- Functionally active biologic

Competitive or collaborative (file for IP if desired)

Industry | Product Development Partner

- Clinical candidate (compound or biologic)

IMPACT OF SGC CHEMICAL PROBES

SGC CHEMICAL PROBES BY THE NUMBERS

DISCOVERED

173+

Novel chemical probes developed in collaboration with industry and academic partners

DISTRIBUTED

42,662+

Samples of chemical probes distributed globally by SGC and trusted vendors

CITATIONS

10,000+

SGC chemical probes used by scientists around the world

CLINICAL TRIALS

50+

Clinical trials and late-stage preclinical programs based on therapeutic hypotheses generated with SGC chemical probes

HUNDREDS OF PAPERS USING SGC PROBES RESULTING IN THERAPEUTIC HYPOTHESES

SGC Take-home Lessons

Industry interest tracks with more openness

SGC

2004 — 2007 — 2011 — 2015 — 2020 — 2025

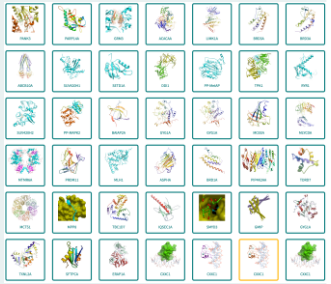
PHASE I | Phase II | Phase III | Phase IV | Phase V

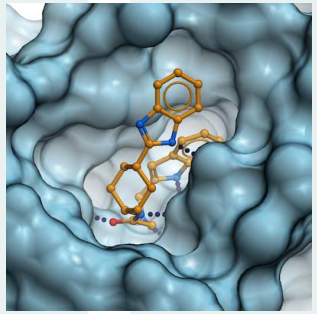
SCIENTIFIC FOCUS

STRUCTURAL GENOMICS

Human Protein Families

Human Parasite Proteins





CHEMICAL GENOMICS

Bio-active Chemical Tools

TARGET 2035

DATA DRIVEN DD

Machine Learning

Patient-derived disease assays

INDUSTRY PARTNERS

GlaxoSmithKline

GlaxoSmithKline, Pfizer, MERCK, NOVARTIS

GlaxoSmithKline, Takeda, Pfizer, janssen, Lilly, abbvie, Boehringer Ingelheim, BAYER, NOVARTIS

Takeda, Boehringer Ingelheim, janssen, MERCK, Pfizer, BAYER, abbvie, MSD, NOVARTIS

Genentech, janssen, MERCK, Pfizer, Boehringer Ingelheim, Takeda, BAYER, Bristol Myers Squibb

CONSORTIA PROVIDE EXCELLENT TRAINING ENVIRONMENTS

- **Winner of the 2021 Mitacs Award for Exceptional Leadership - Industry**

Melissa Landon
Chief Strategy Officer
Cyclica, Canada

Fabien Marino
Vice President Industrial Affairs & Site Head
Sanofi, Toronto, Canada

Sujata Sharma
Global Head, Protein and Structural Sciences,
Janssen R&D, PA

Anthony Bradley
VP, Design Development
Exscientia, UK

Kong Nguyen
VP, Computer Aided Drug Design, **Atomwise, CA**

Ekatarina Kusnetsova
Director of Product Development,
Reaction Biology Corporation, PA

SGC CANADA-WIDE INDUSTRY PARTNERED TRAINING PROGRAMS

Mitacs

NSERC CRSNG

CREATE PROGRAM

Open science leads to many spin-offs

Community Initiatives

Chemical Probes Portal

Online resource to promote best practices in chemical biology and drug discovery

Target 2035: Towards Medicines for All

A pharmacological modulator for each human protein by 2035

CACHE: Critical Assessment of Hit Finding Experiments

To benchmark and enable the best methods for prediction of protein-ligand binding

Pandemic prevention projects

Non-profits to coordinate our anti-viral discovery efforts

Commercial spin-offs: Ability to translate open science to the market

WDR5 Open Science Drug Discovery Program

$1B deal between OICR & Celgene with a commitment to ongoing clinical development in Canada

An open science spin-off drug development company

$4M raised to develop effective therapeutic treatment for rare pediatric brain cancer

YCharOS: Open science characterization of antibodies

$2M+ in inward investment to Canada and awarded the **"2021 Irv and Helga Cooper International Open Science Prize"**

Structure-Guided Drug Discovery Coalition

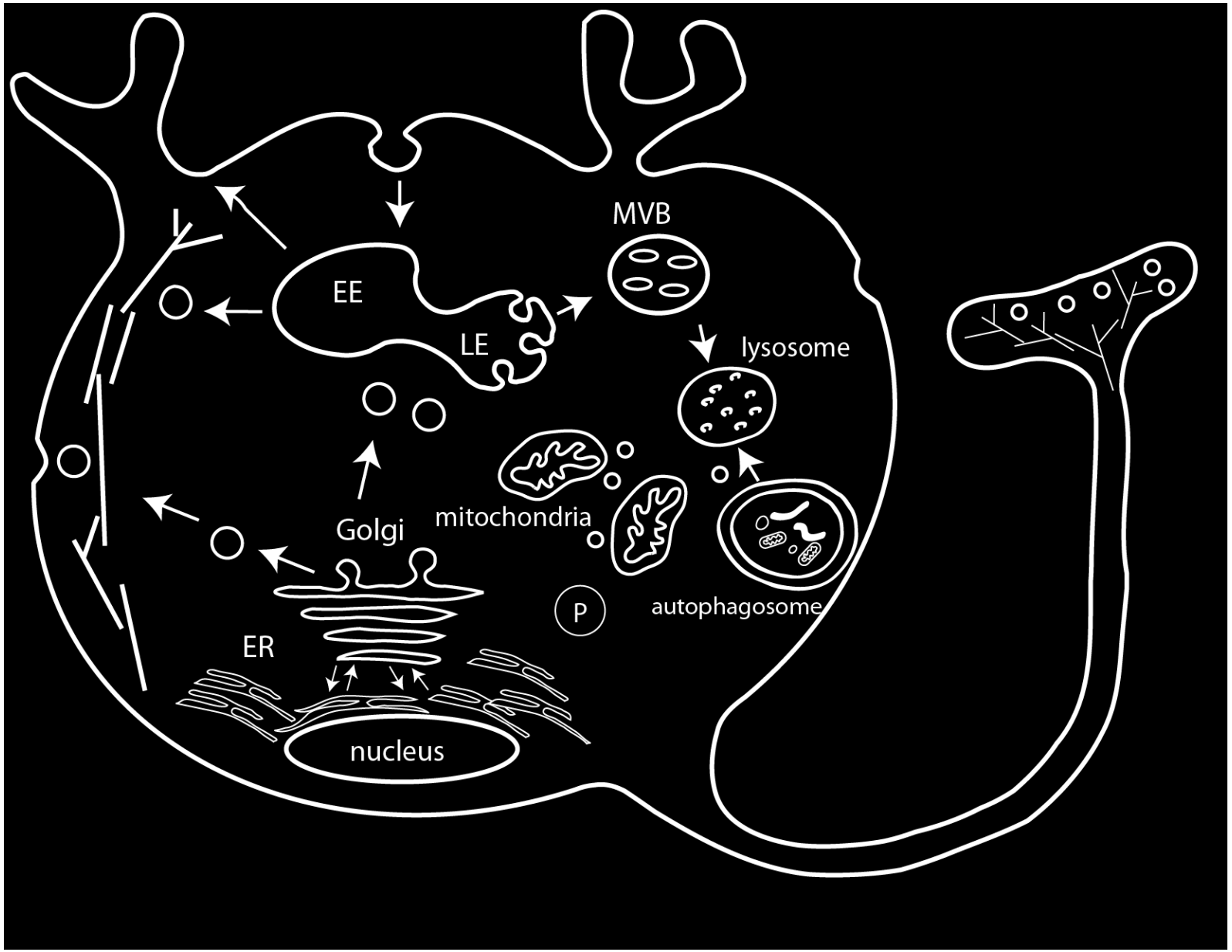
Malaria enzyme lysyl-tRNA synthetase project awarded the **"2018 MMV Drug Discovery Project of the Year"**

A NON-PHARMA CONSORTIUM

Antibodies

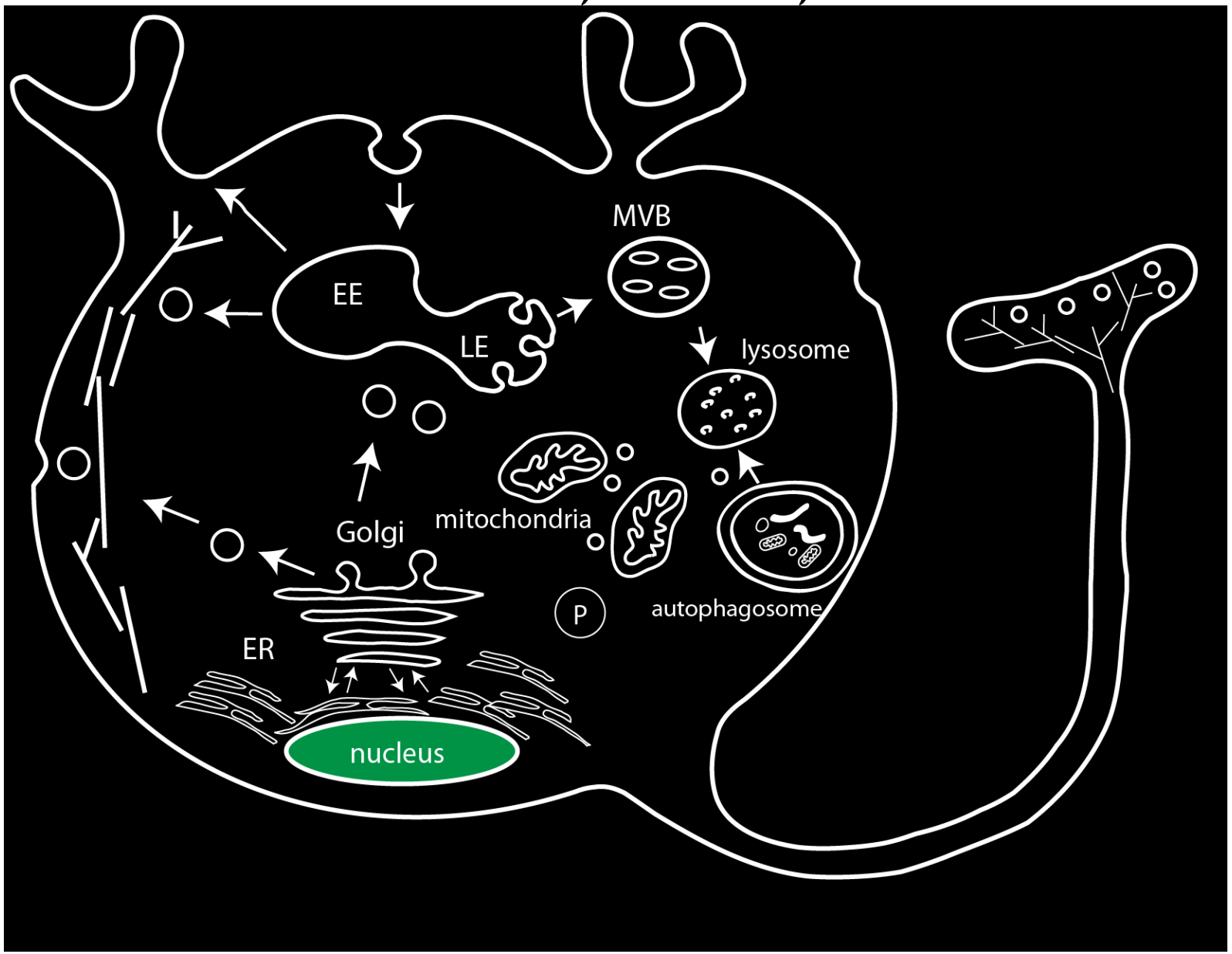
Among the most common reagents used in biomedicines

Antibodies can be used to discover where proteins are in the cell

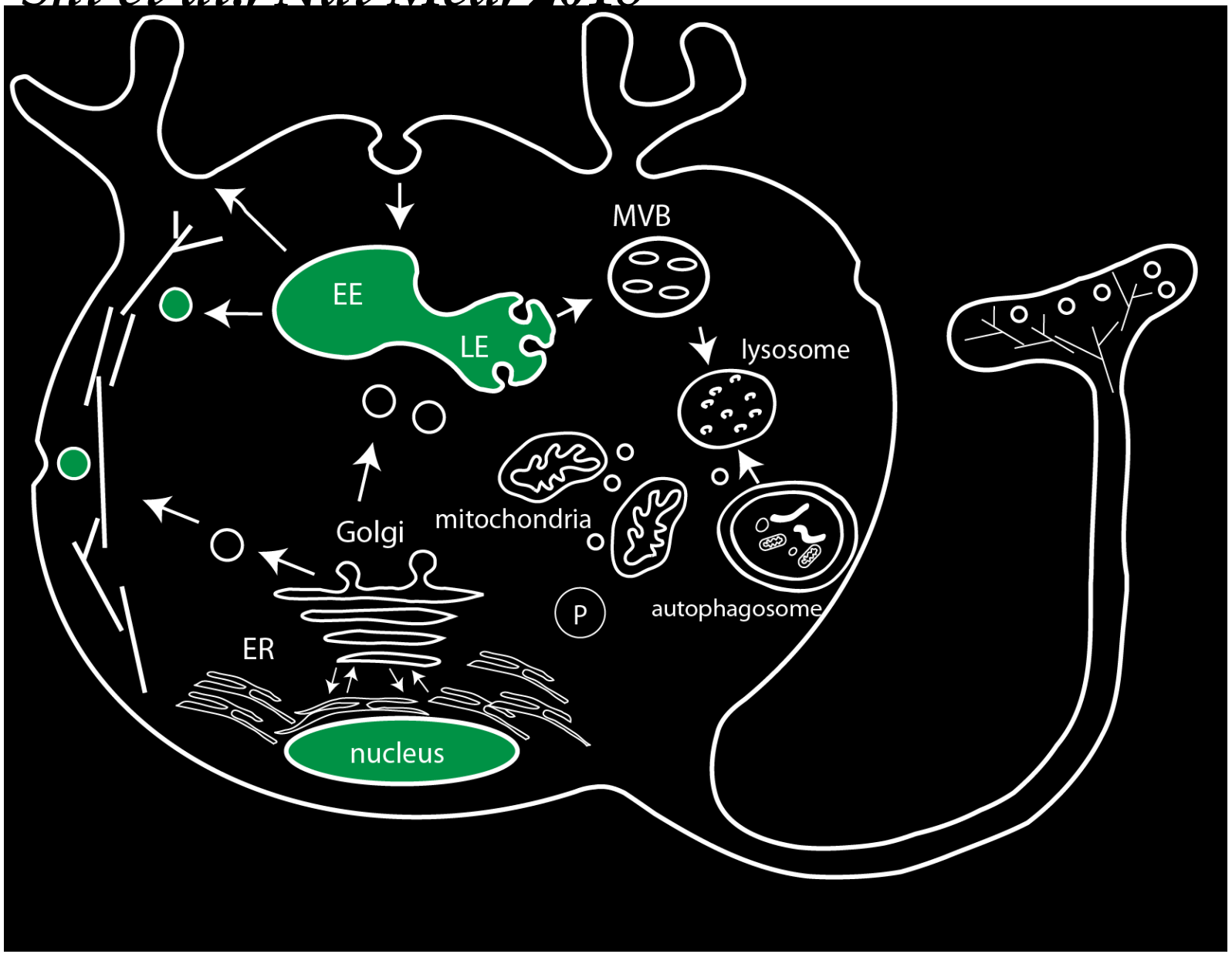


Where is C9ORD72?

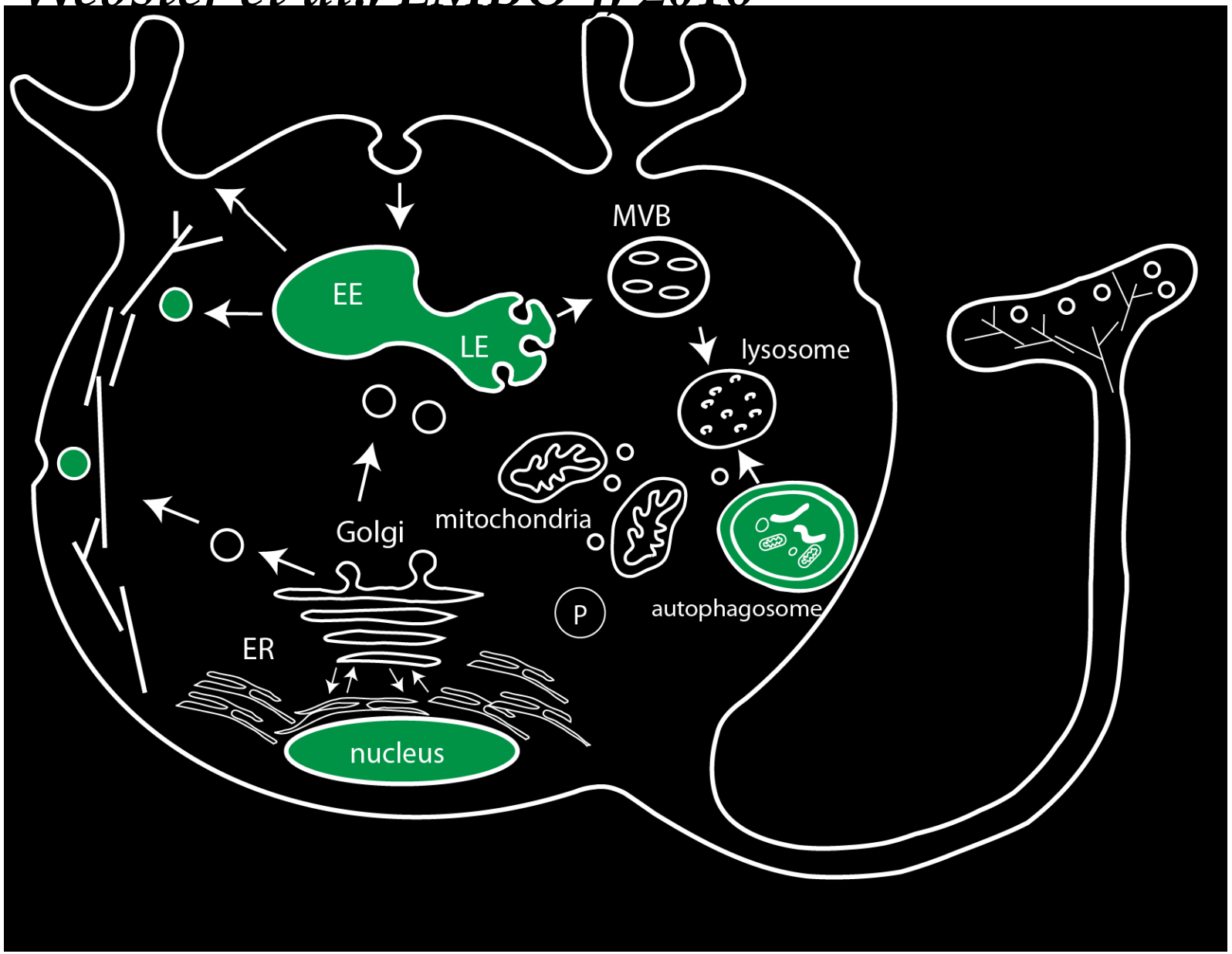
Renton et al., Neuron, 2011



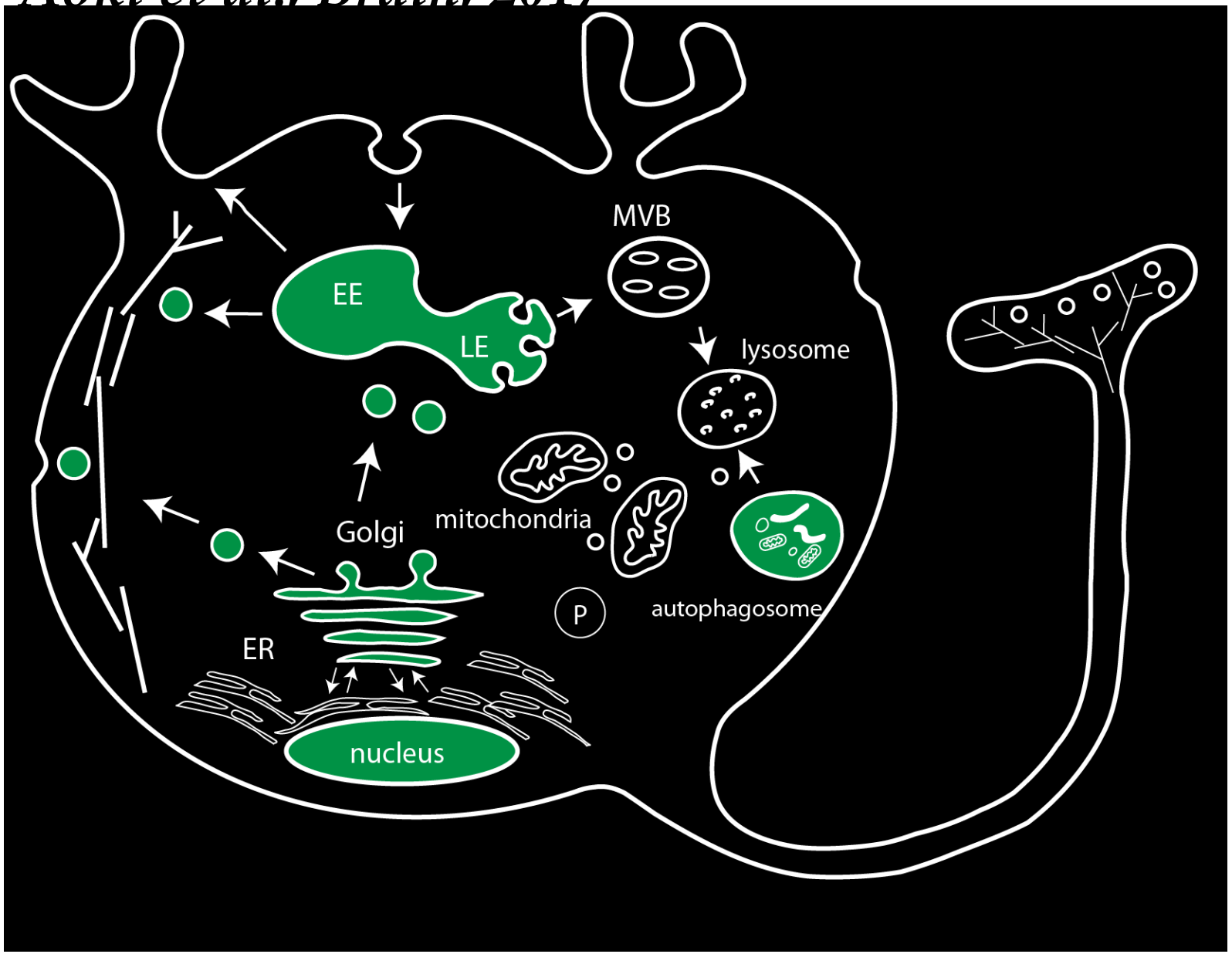
Farg et al., Hum Mol Genet, 2014
Shi et al., Nat Med, 2018



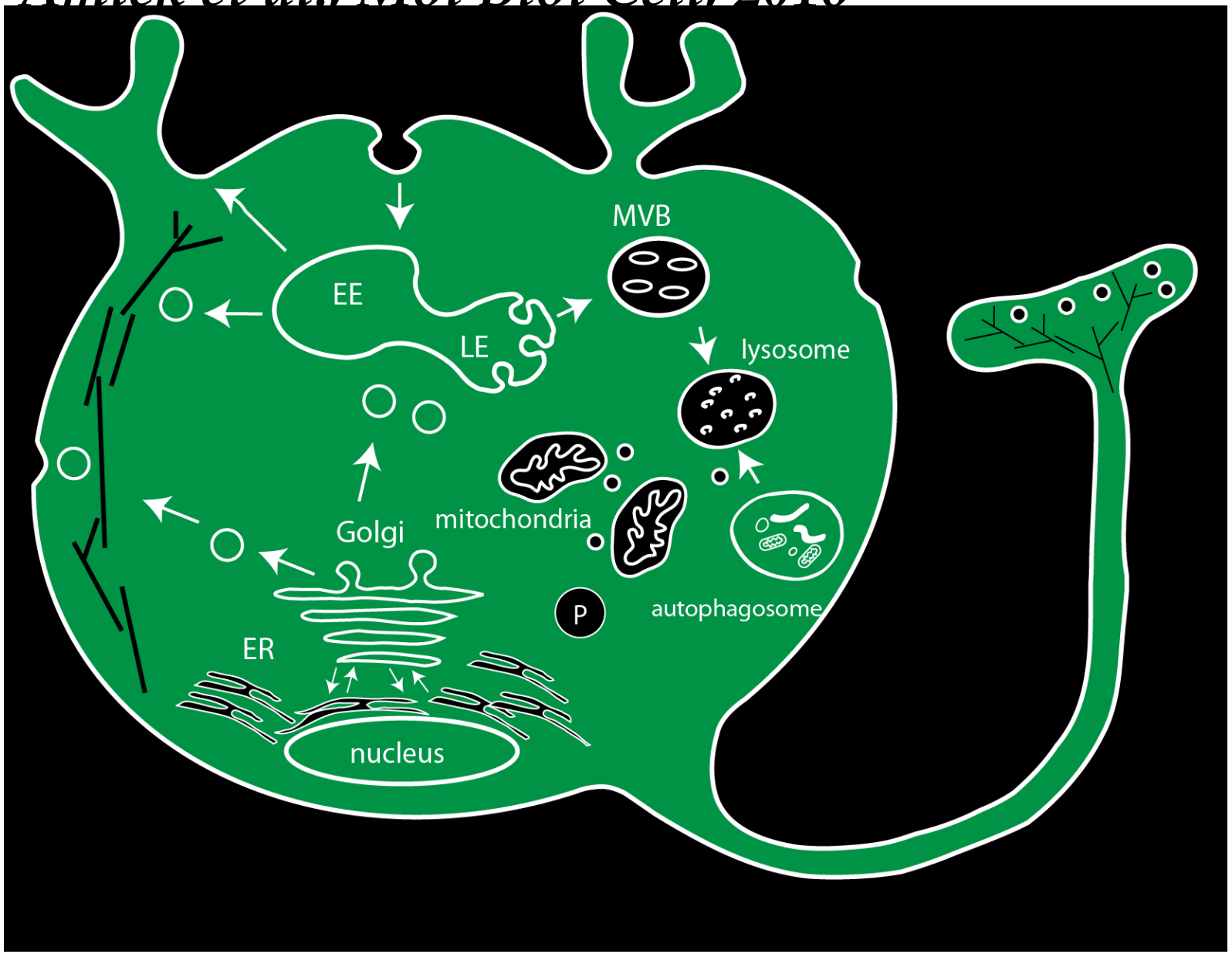
Webster et al., EMBO J, 2016



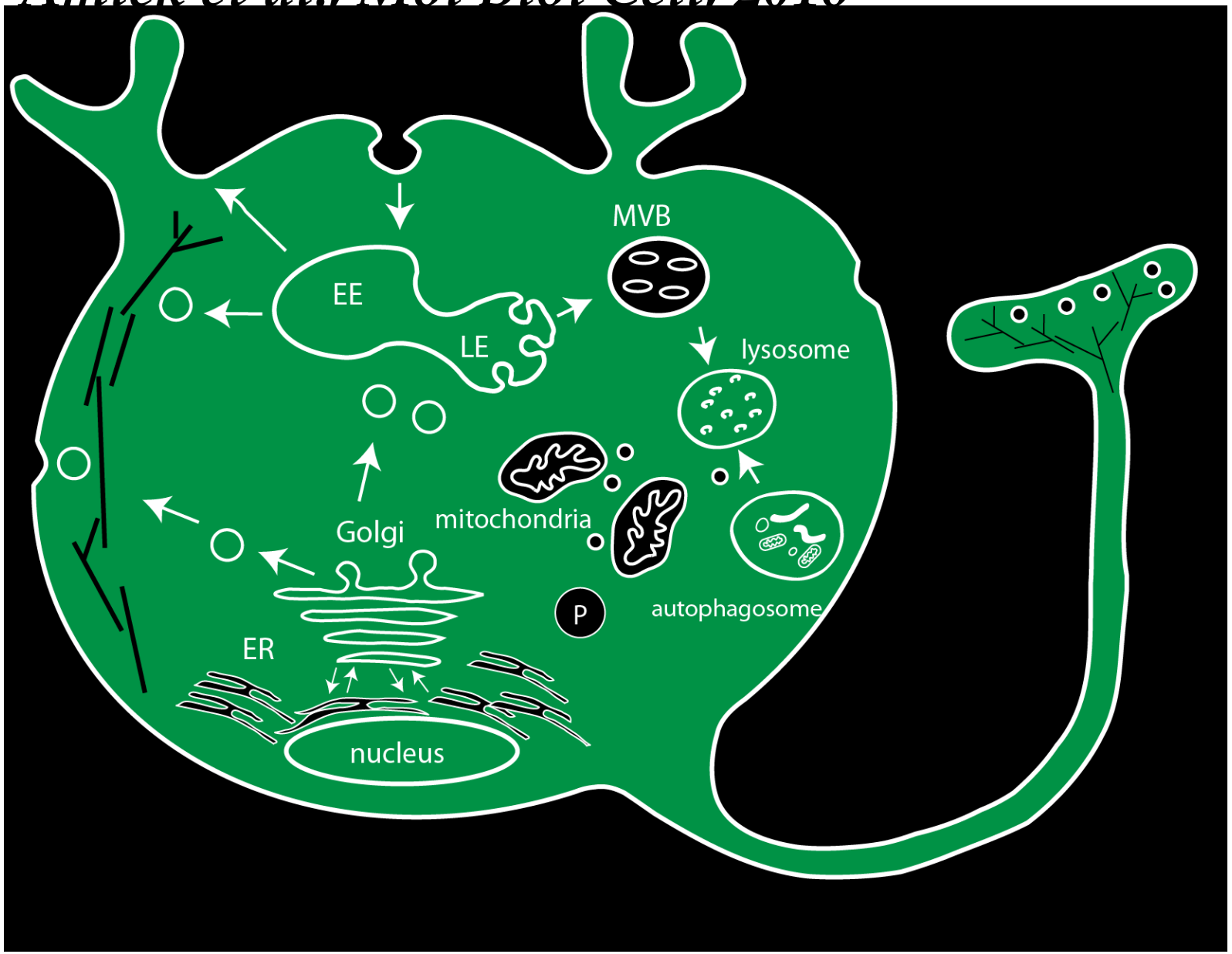
Aoki et al., Brain, 2017



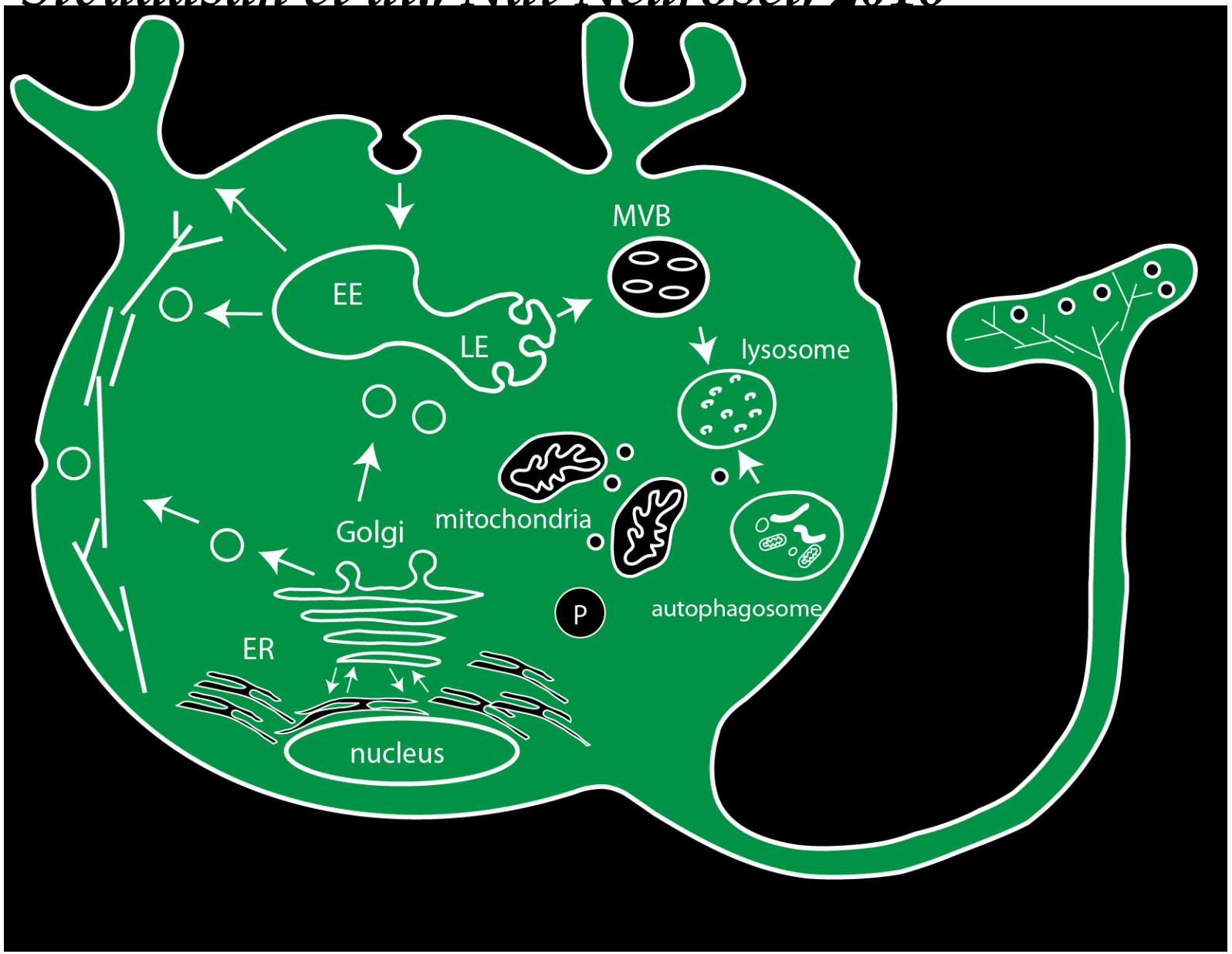
Yang et al., Sci Adv, 2016
Amick et al., Mol Biol Cell, 2016



Amick et al., Mol Biol Cell, 2016



Sivadasan et al., Nat Neurosci, 2016

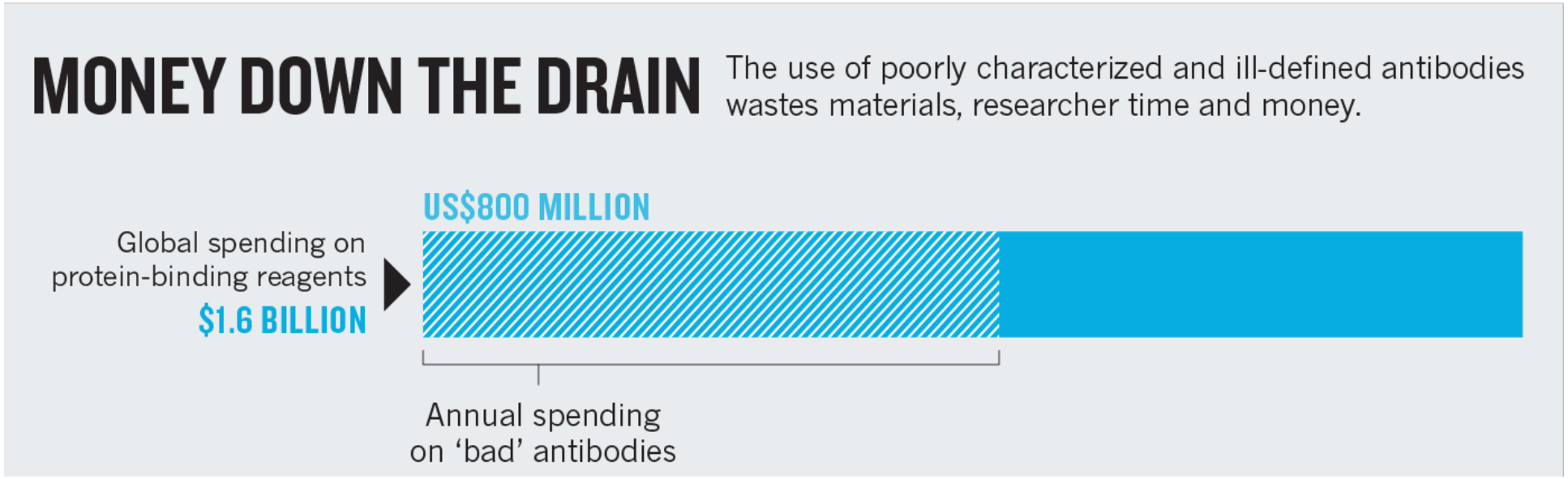


WTF?

It’s the antibodies, dummy.

Quality reagents – the foundation of good science

Reproducibility crisis: Blame it on the antibodies
Baker, *Nature*, 2015



Bradbury and Pluckthun, *Nature*, 2015

This been a “wicked” problem for >30 years

Industry

- It costs $30,000 to characterize an antibody properly, but only 10% of the antibodies in their catalogues generate $1,500 in revenue
- There are also no community-accepted quality criteria to work toward

Academia

- Few labs have skill sets or resources to characterize antibodies properly
- They expect industry to QC their products

Funders and journals

- Reticent to impose criteria on their constituents
- Looking for community to come up with solution or standards

There have been some (failed) attempts at finding a solution

- Create new antibodies (though >1 million available)
- One community effort tried to impose quality criteria on industry
- Journals asking for evidence of characterization

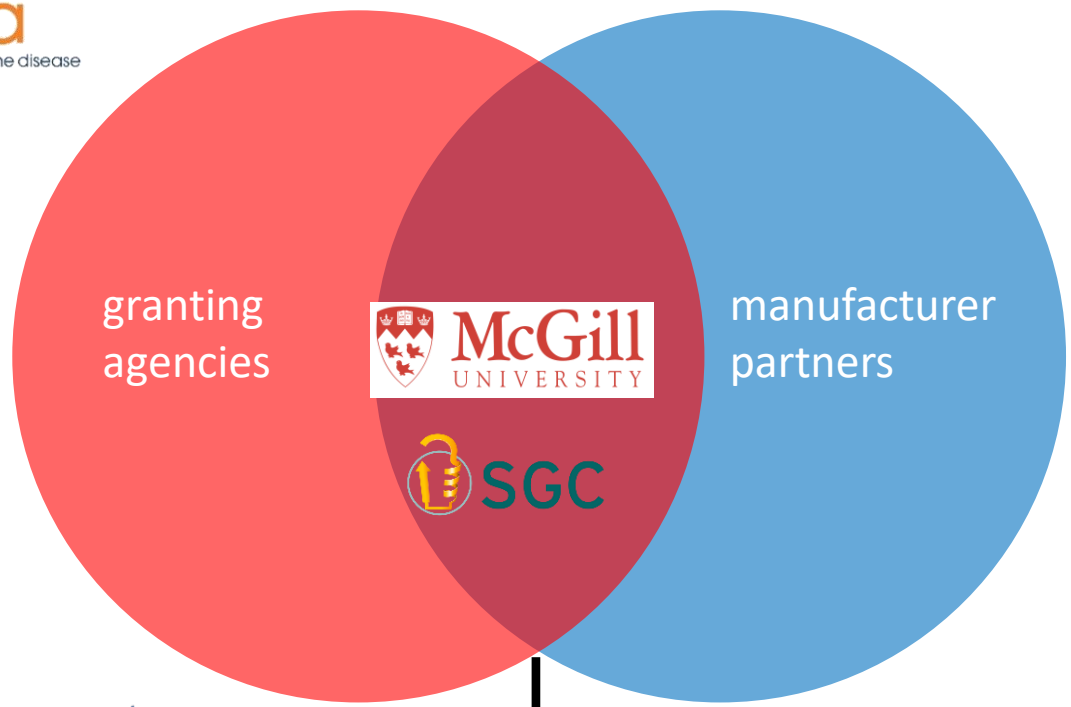
YCharOS Consortium - process and concept

- Many companies want to do the right thing
- Concept to work with these industry partners to create a common characterization platform that can test company products in parallel (more cost-effectively)
- Get buy-in from a few industry partners to start, and then expand
- Organize as an open science initiative
  - Sends clear message that the effort will not change business model and try to monetize the science

YCharOS governance

- Gain trust with monthly calls with industry partners to go over data, and to design strategy
- Industry contributes funding, and massive in-kind
- All data made available on Zenodo, without restriction (including the right of companies to use the data for marketing)

How is our “cunning plan” going?



Data placed on Zenodo, an open access data sharing site CERN
https://zenodo.org/communities/ycharos/
https://ycharos.com/

YCHAROS
ANTIBODY CHARACTERIZATION THROUGH OPEN SCIENCE

- Total # of public antibody reports: **48**
- Total # of antibodies tested: **432**
- In-kind contribution to the project: **~$1.3m USD**
- Cash funds obtained so far: **~$3.2m USD**

Other open science university/industry consortia to ask me about

- CACHE – Benchmarking AI in drug discovery (SGC and ~10 companies)
- Open Plastic - Plastic degradation (Three universities and 4 companies)
- Pulp and Paper Consortium – Training in this sector (Toronto and >10 companies)