LUXEMBOURG INSTITUTE OF HEALTH
RESEARCH DEDICATED TO LIFE

Center for quantitative biology

Prof. Dr. Gunnar Dittmar

Center for quantitative clinical biology

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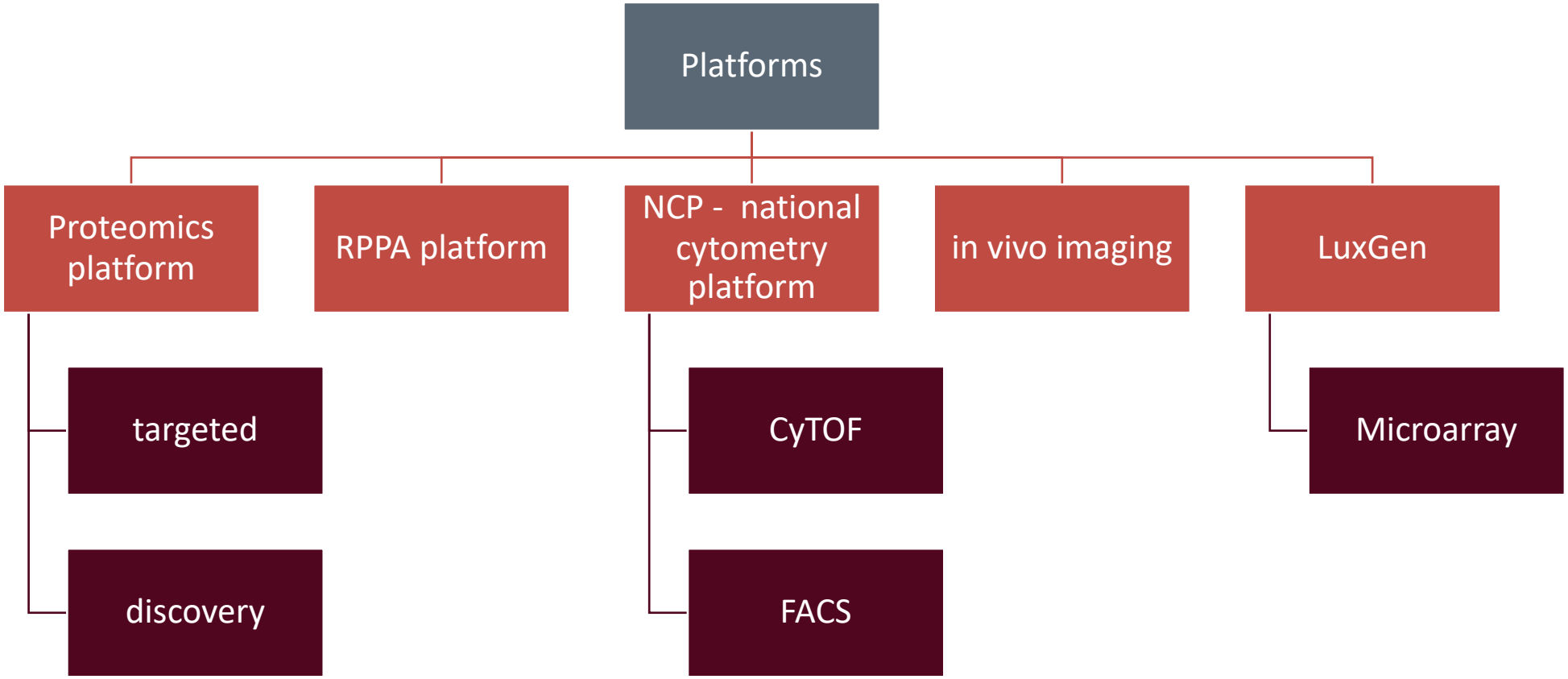
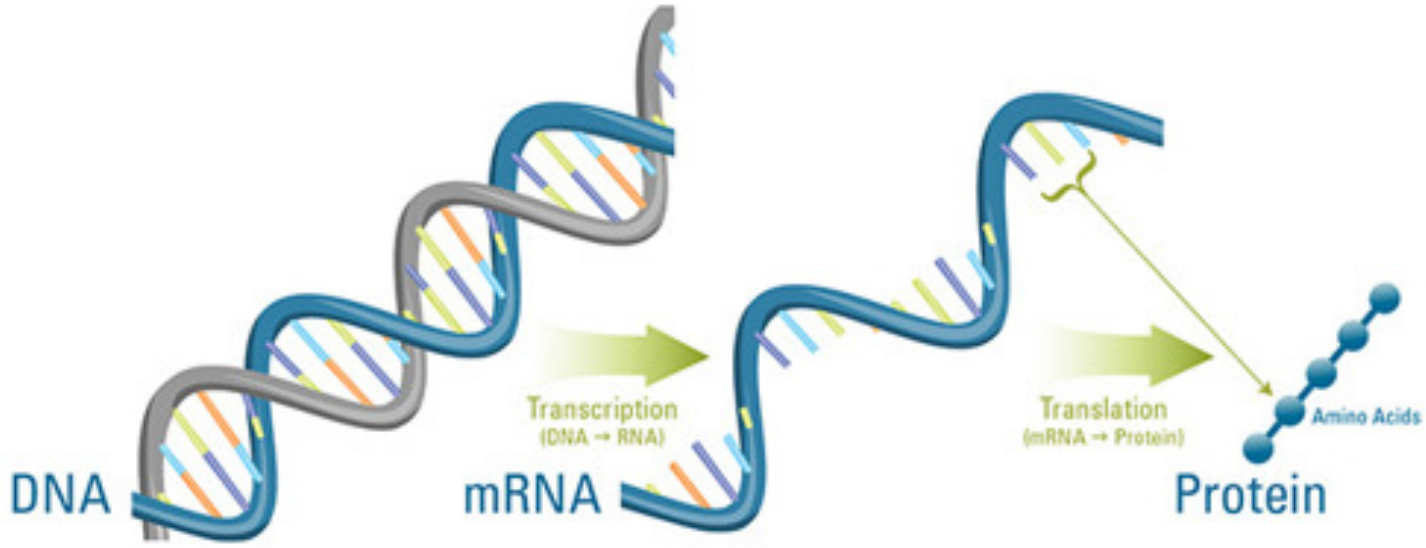


Measurement techniques



Deep Sequencing
Next generation sequencing

Microarray
RNASeq

Proteomics
RPPA

Genomics

Proteomics

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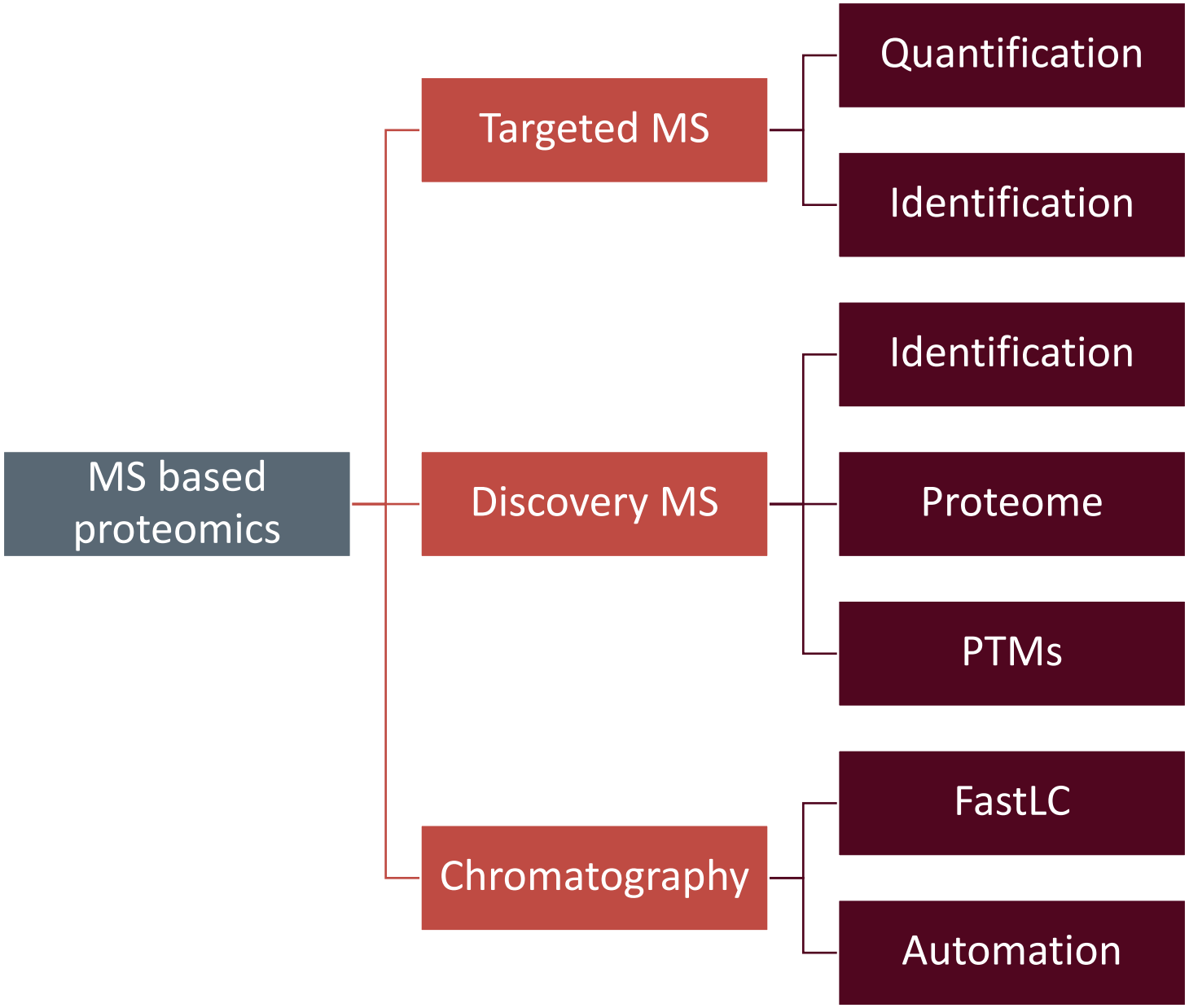
Proteomics



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Targeted vs. shotgun proteomics

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Targeted proteomics

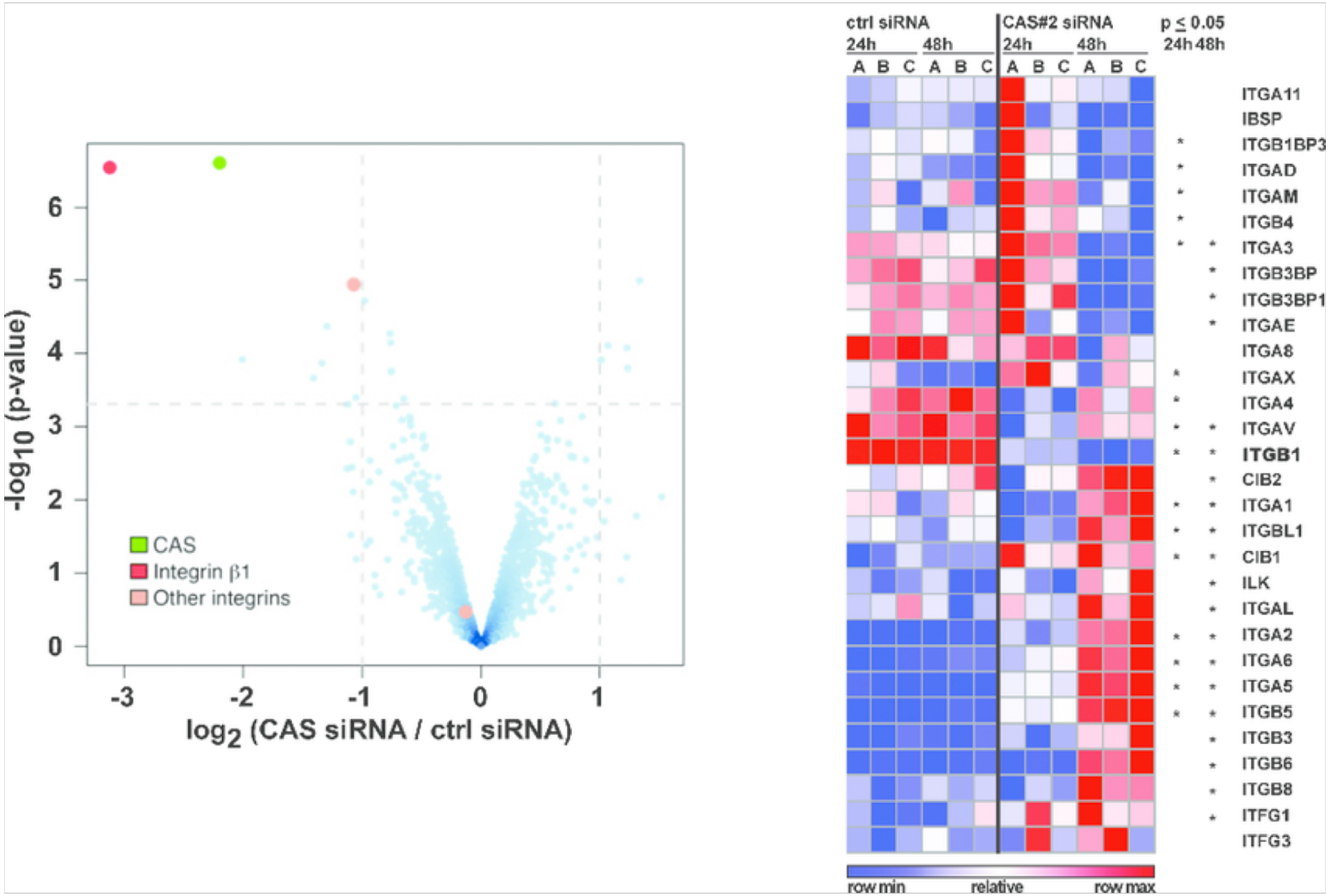
- Reliable quantification in each sample
- Limited number of proteins
- High sensitivity

- Can be applied on large sample sets

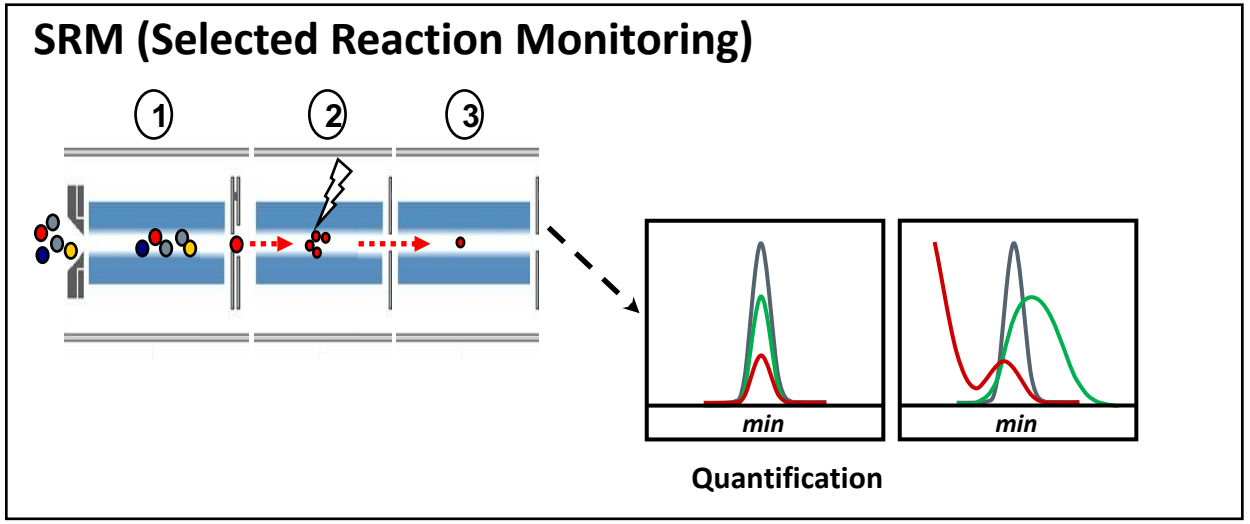
Shot-gun

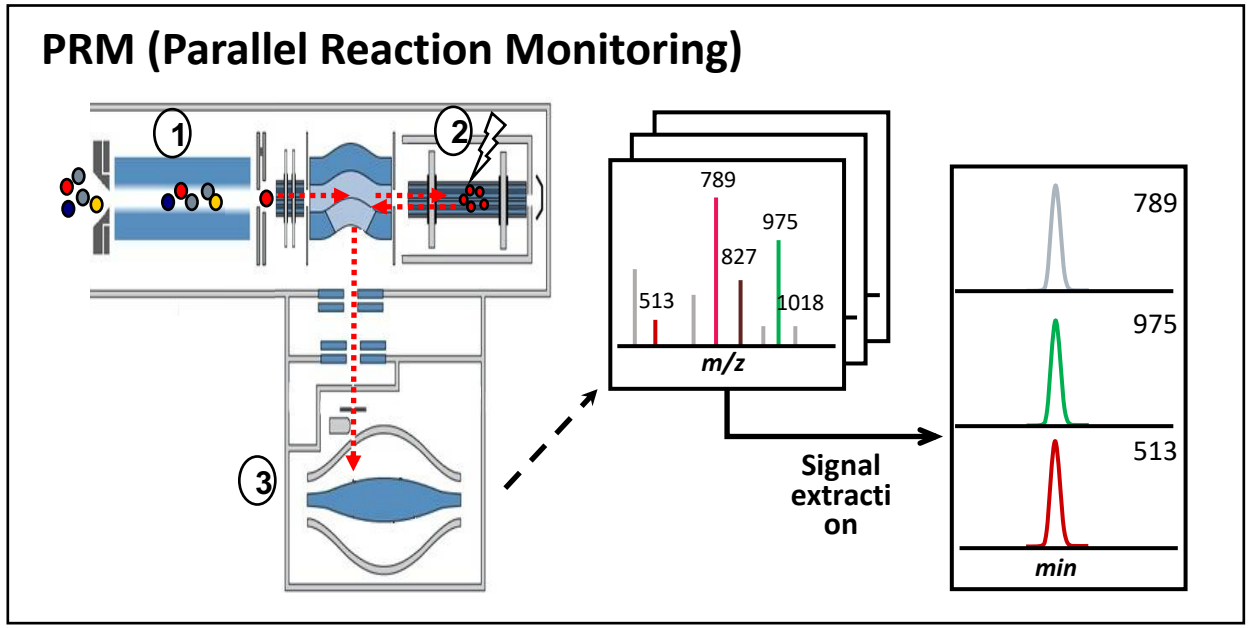
- Deep analysis of samples
- Discovery of new proteins and modifications

Discovery analysis of two proteomes



Implementation of PRM





Advantages

Higher selectivity by HRAM

Flexibility by various parameters

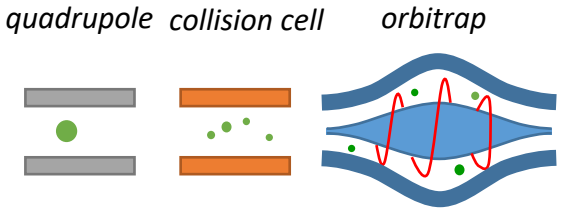
Post-acquisition data analysis

Scheduled PRM

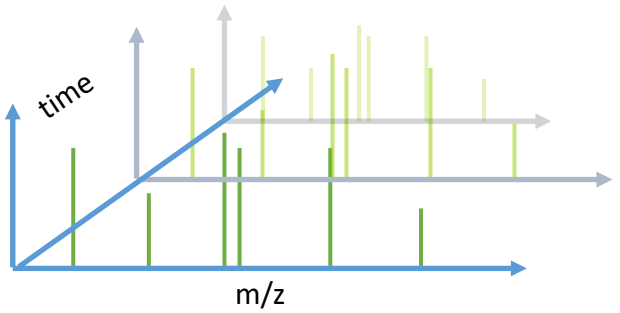
isPRM

Automated RT correction

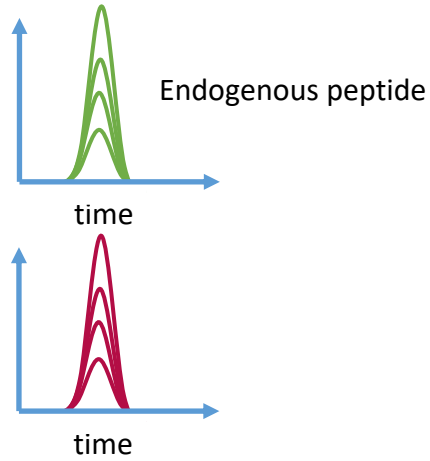
Parallel reaction monitoring



MS2 spectra



Identification/Quantification



- Selectivity
  - High resolution can separate close mass peptides
- Sensitivity
  - Improvement of signal
  - Physical trapping of ion
- Throughput
  - Multiplexing capability (up to 200-300 peptides samples)
  - Fast chromatographic separation (acquisition time from 90 min to 10 min per sample)
  - IS-PRM (up to 500 peptides)
- Robustness
  - Data processing script (spectral matching)
  - Standardization of the sample preparation

Coupling fast liquid chromatography with MS

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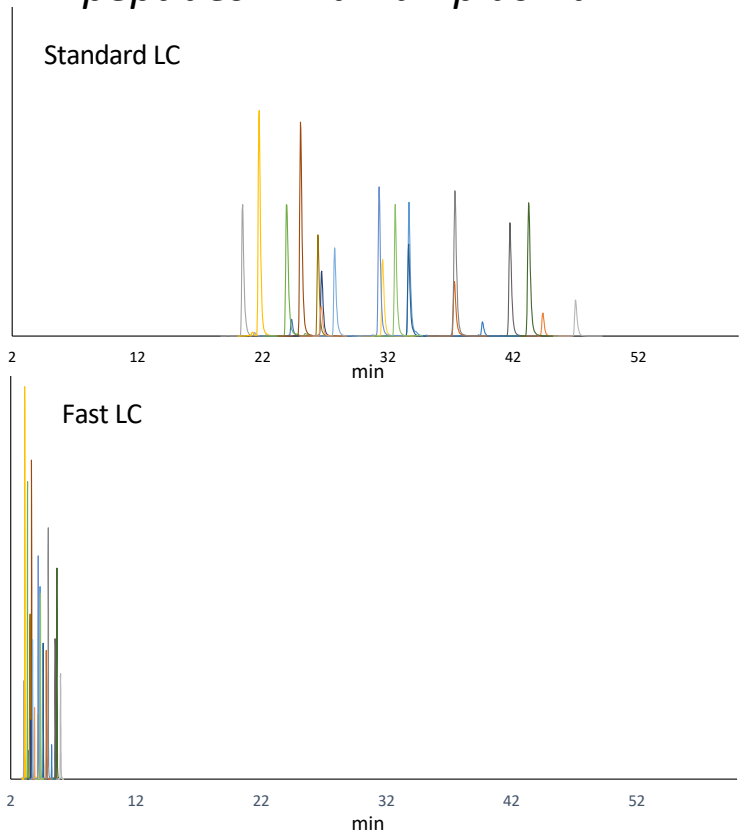
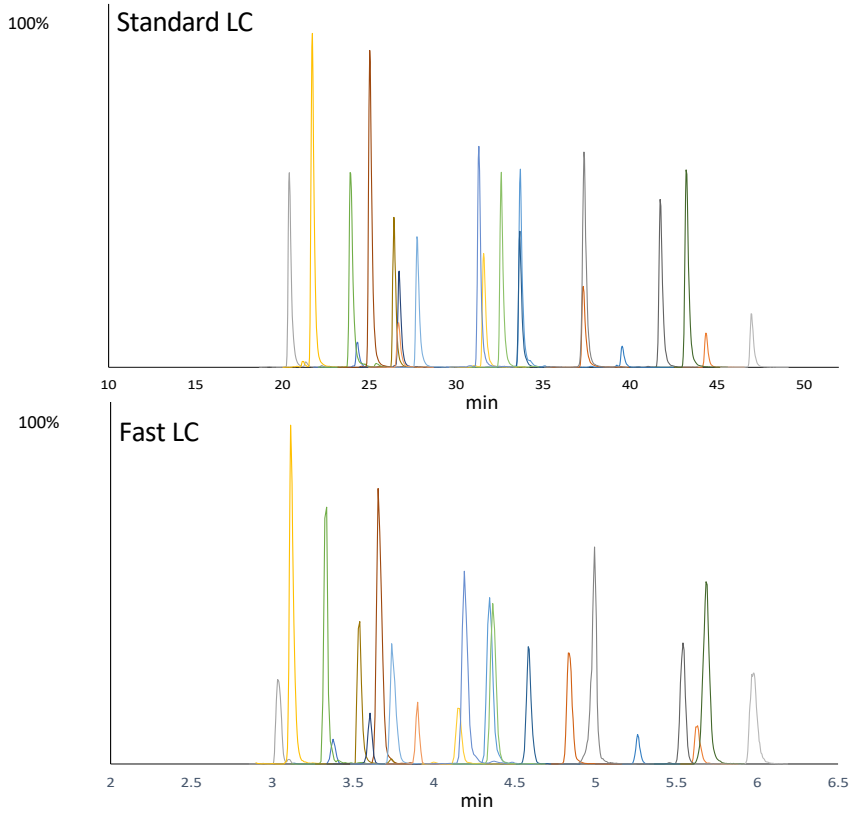
21 peptides in human plasma





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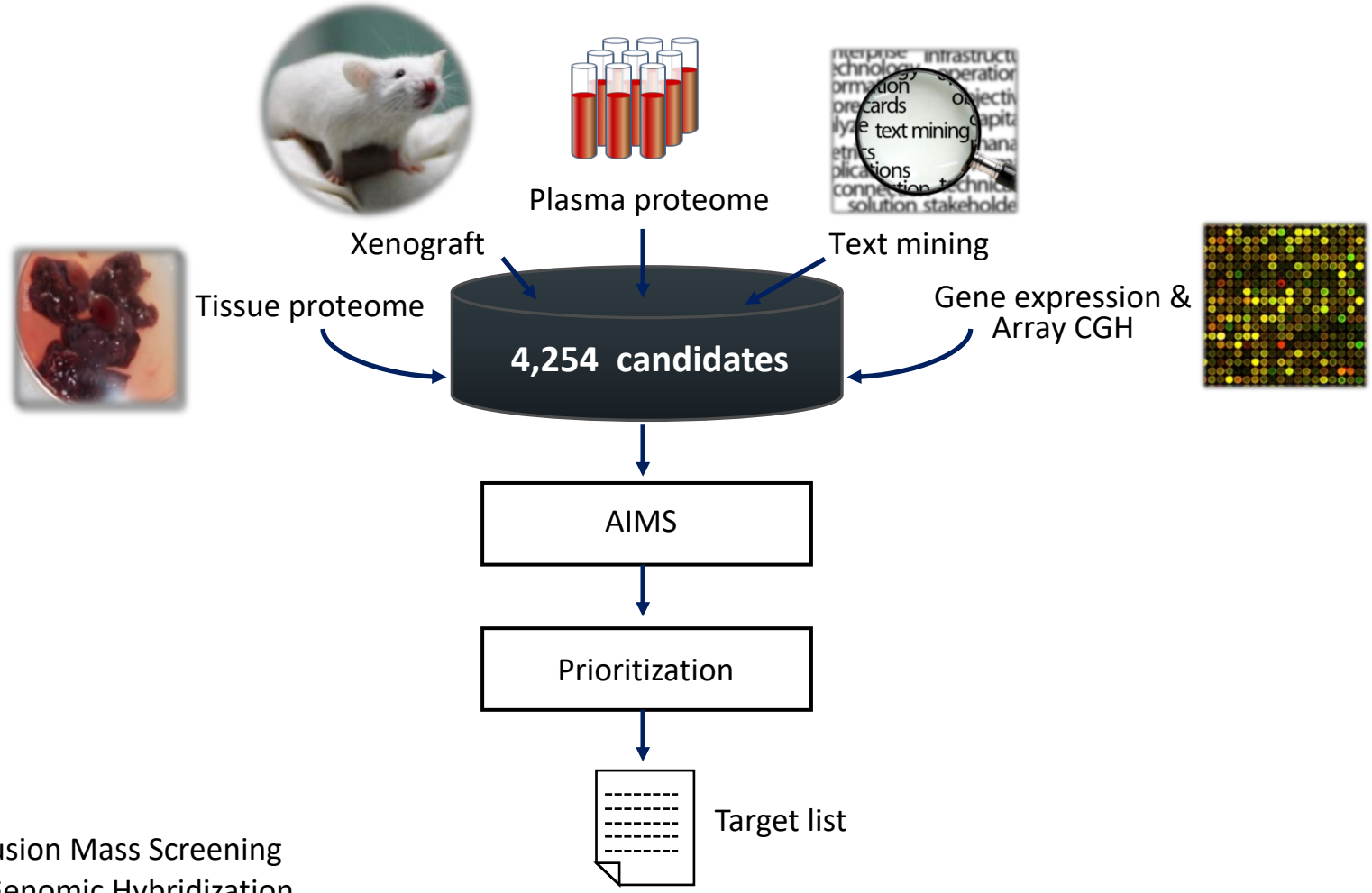
Biomarker Identification

Lung-cancer project and Endometrial cancer

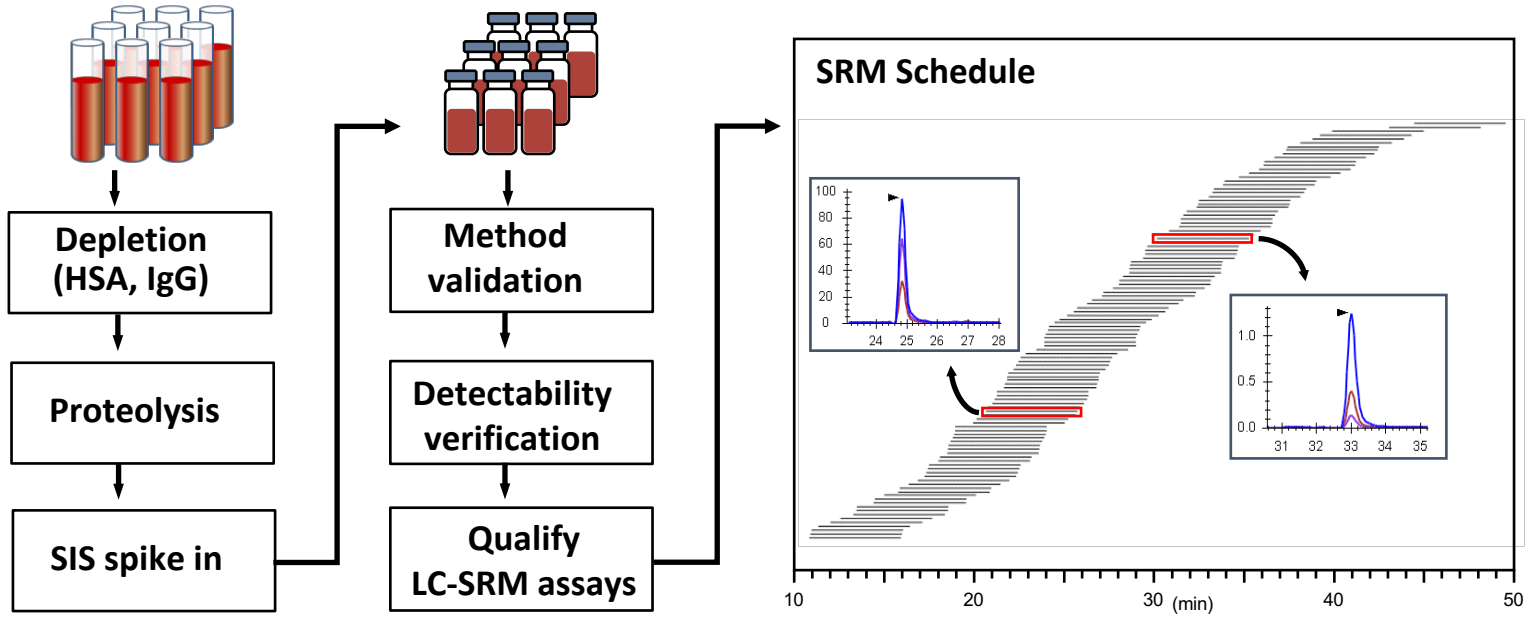
PPM-Lung Cancer: Discovery



AIMS: Accurate Inclusion Mass Screening
CGH: Comparative Genomic Hybridization

Goal: Develop NSCLC biomarkers that can be used for early diagnostics and to stratify patients for precise therapeutics

Targeted Proteomics Workflow



Biomarker Verification in Plasma

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Antibody based proteomics

Reverse Phase Protein Array platform

Protein microarray platform

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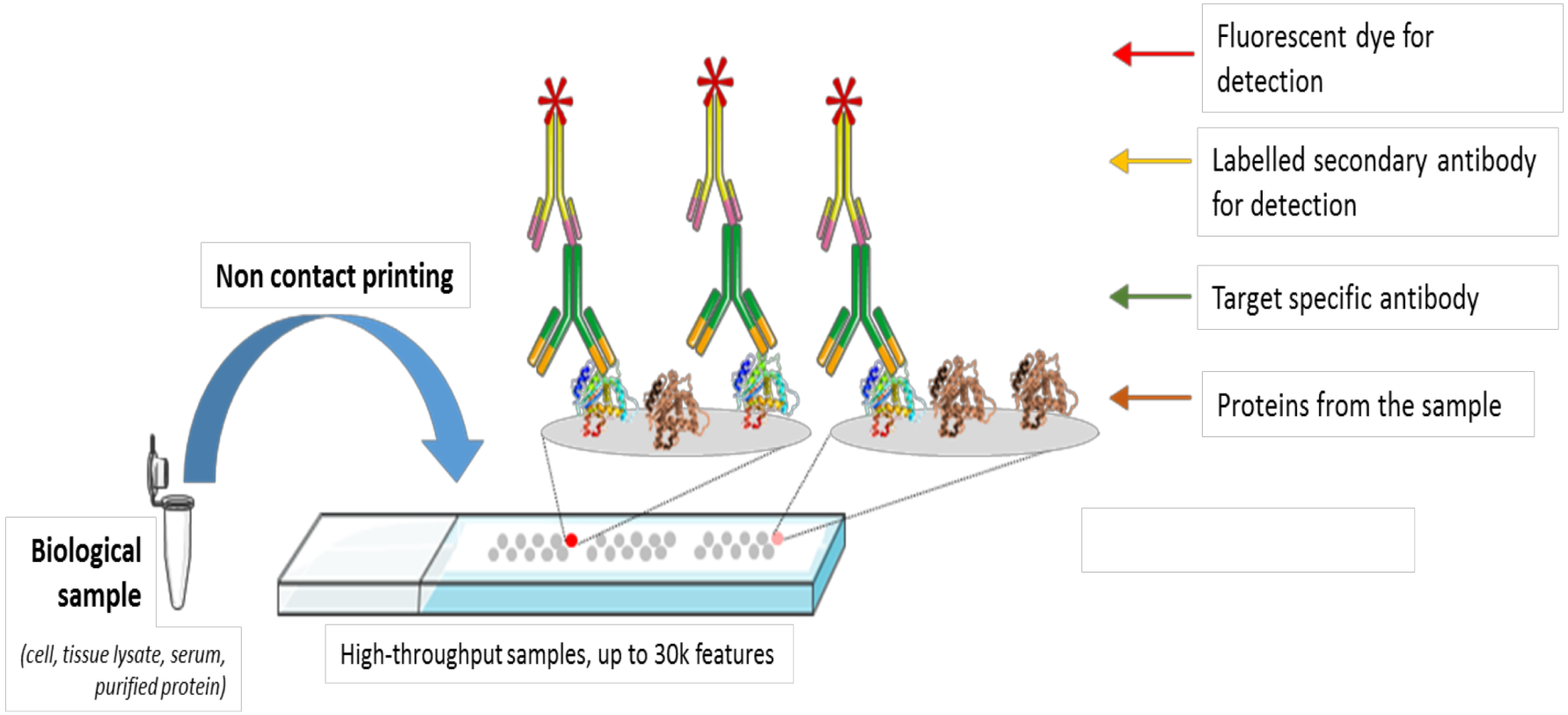
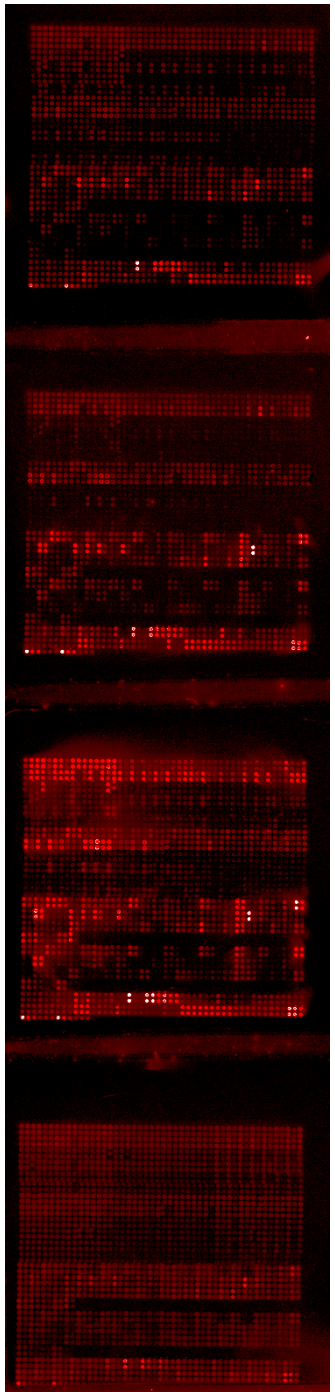
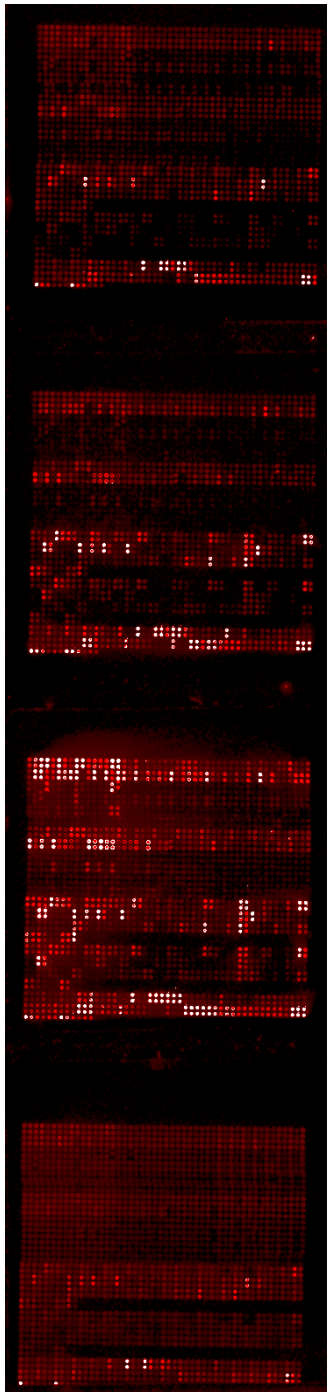


Red scanner



Infra-red scanner



Correlation of signal intensity (F-B) between red and near-infrared scanner

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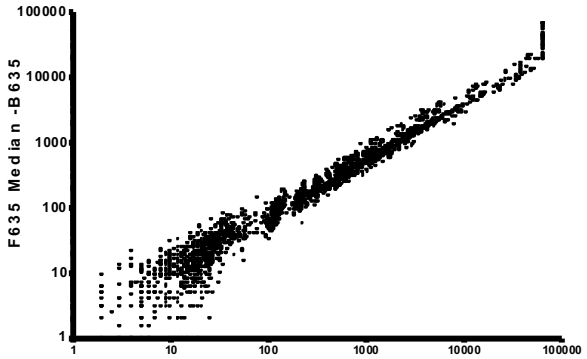
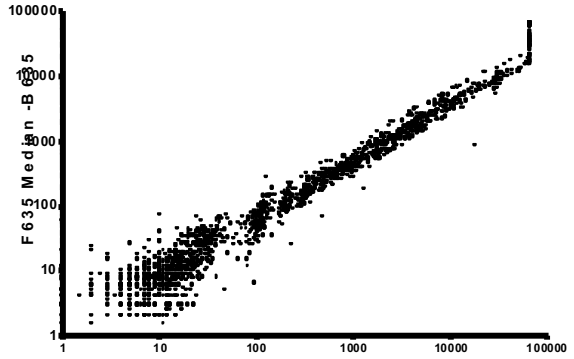
S2-FilaminA



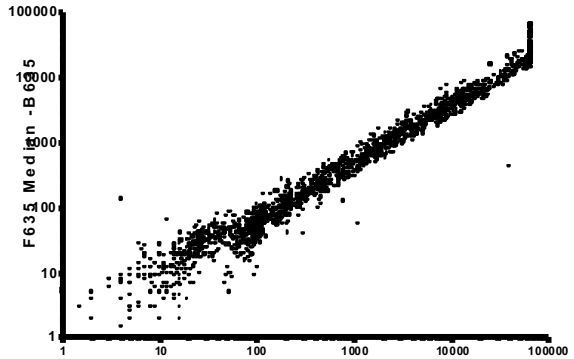
Number of XY Pairs	1972
Pearson r	0.9075
95% confidence interval	0.8993 to 0.9150
P value (two-tailed)	< 0.0001
P value summary	****
Is the correlation significant? (alpha=0.05)	Yes
R square	0.8235

S2-Beta-Actin



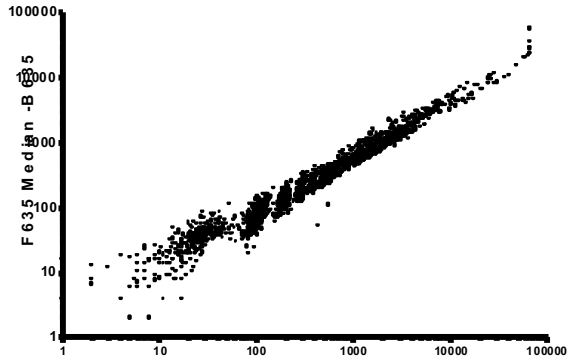
	F635 Median - B635
Number of XY Pairs	1972
Pearson r	0.8831
95% confidence interval	0.8730 to 0.8925
P value (two-tailed)	< 0.0001
P value summary	****
Is the correlation significant? (alpha=0.05)	Yes
R square	0.7800

S2-Alpha-Tubulin



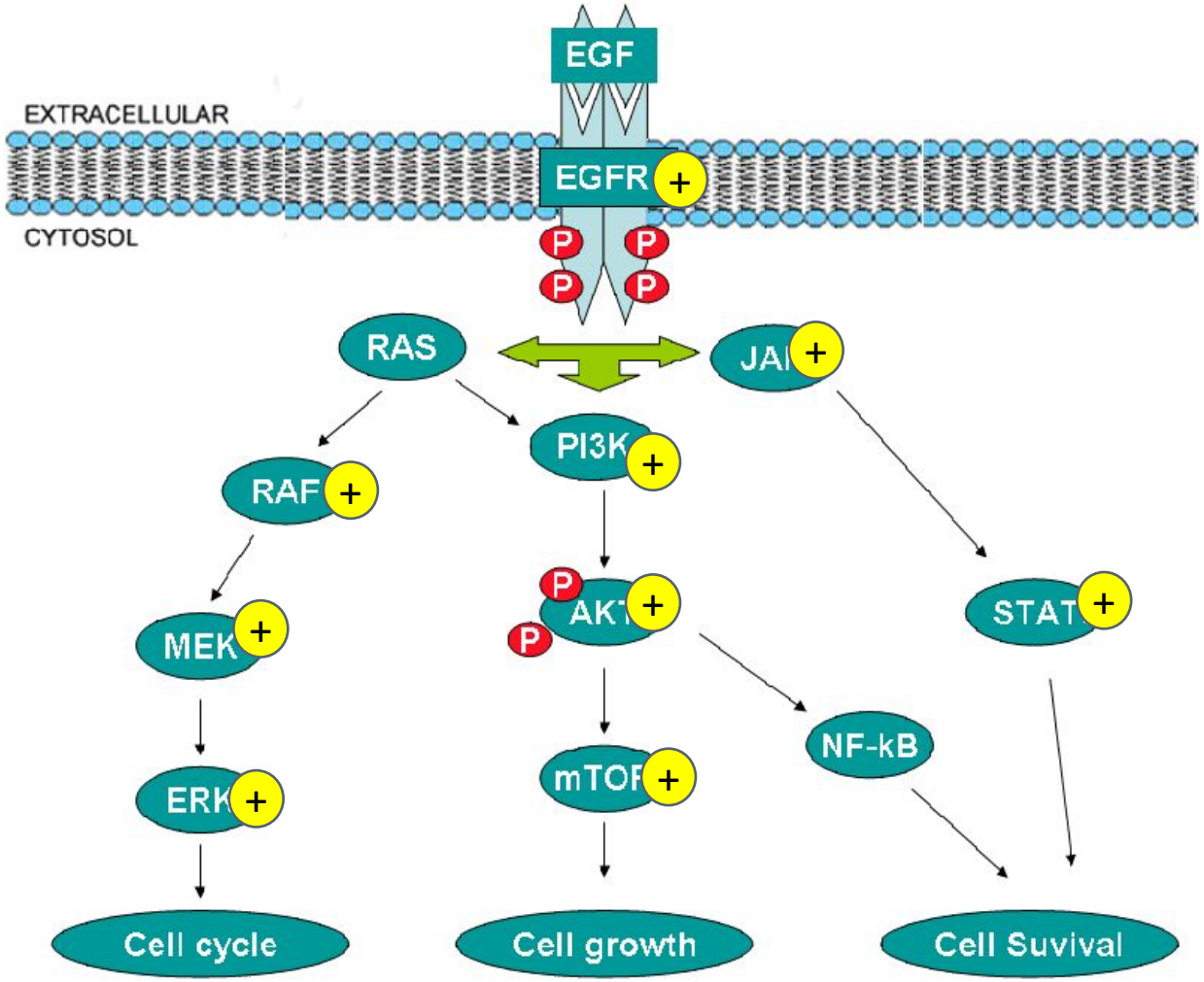
	F635 Median - B635
Number of XY Pairs	1972
Pearson r	0.8872
95% confidence interval	0.8774 to 0.8962
P value (two-tailed)	< 0.0001
P value summary	****
Is the correlation significant? (alpha=0.05)	Yes
R square	0.7871

S2-Vinculin



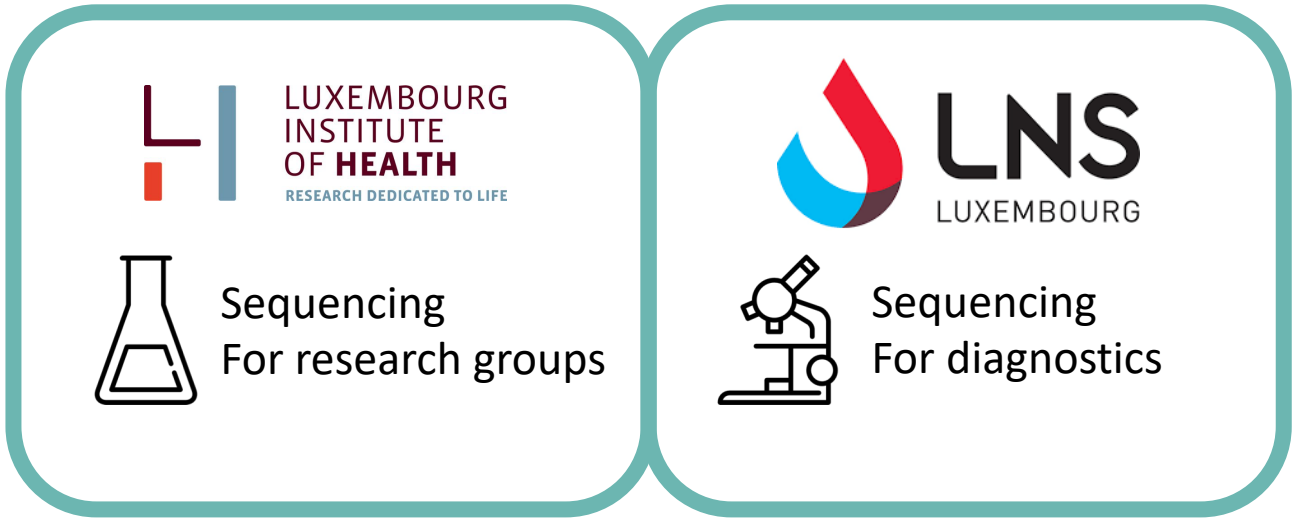
	F635 Median - B635
Number of XY Pairs	1972
Pearson r	0.9235
95% confidence interval	0.9167 to 0.9297
P value (two-tailed)	< 0.0001
P value summary	****
Is the correlation significant? (alpha=0.05)	Yes
R square	0.8529

RPPA for mapping receptor signalling

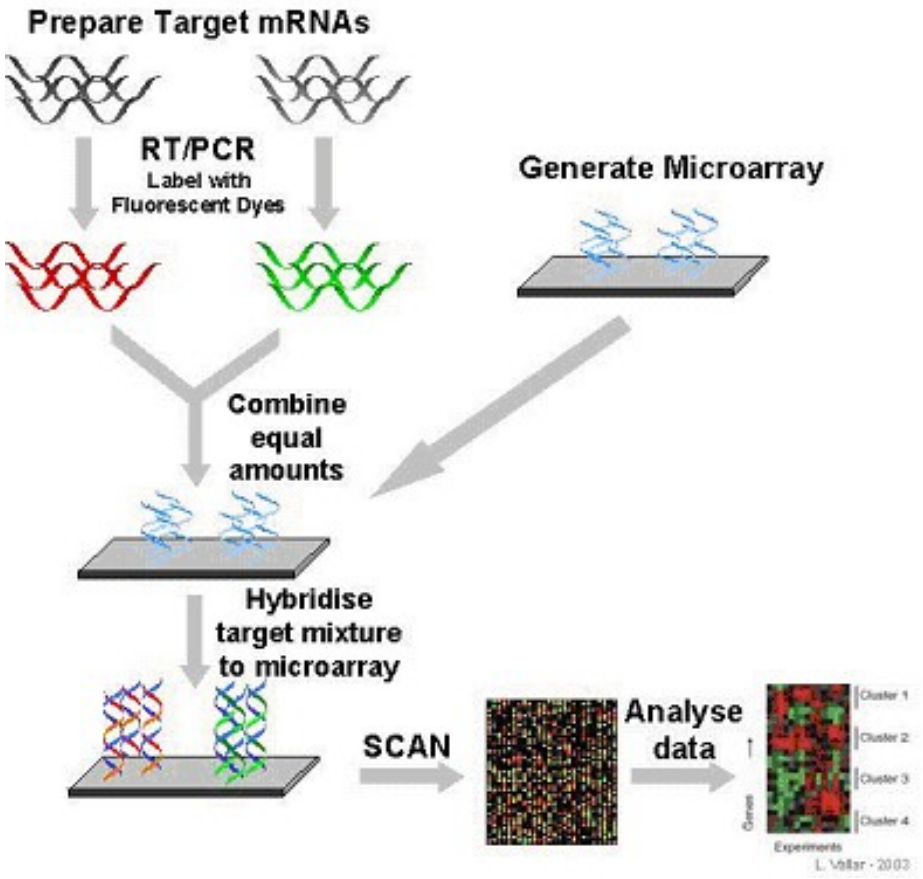


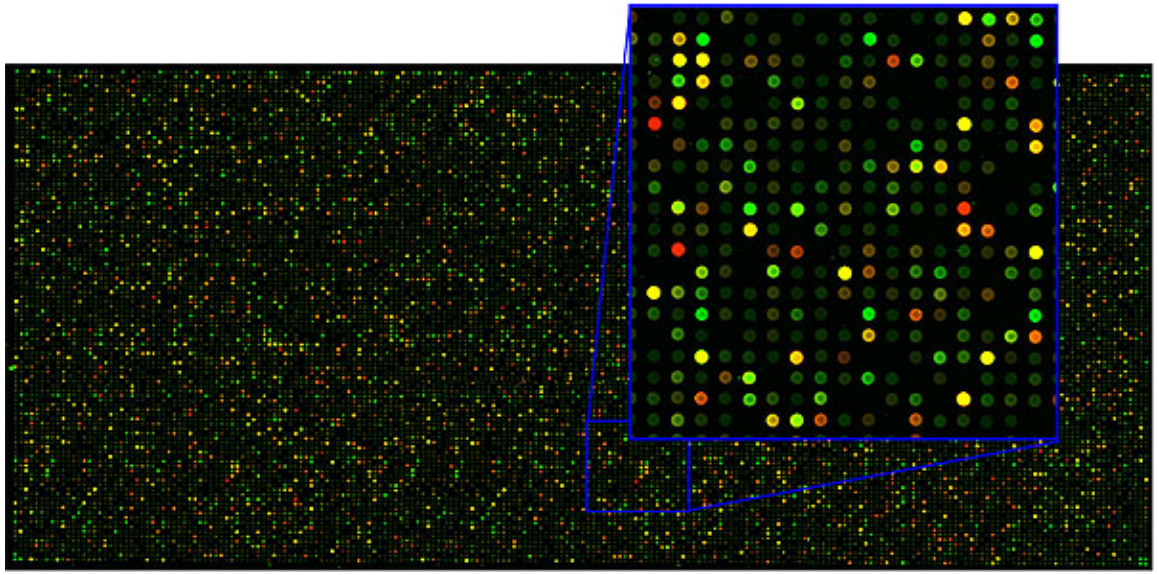
LUXGEN
NEXT GENERATION SEQUENCING

LUXEMBOURG INSTITUTE OF HEALTH
RESEARCH DEDICATED TO LIFE



Transcriptomics





Analysis of all human known transcripts.

Contact

LUXEMBOURG INSTITUTE OF HEALTH
RESEARCH DEDICATED TO LIFE

Proteomics

Dr. Antoine Lesur

proteomics@lih.lu

RPPA

Dr. Joseph Longworth

rppa@lih.lu

Microarrays

luxgen@lih.lu

Clinical Research in Luxembourg: Achievements and future challenges

2019/01/23

Myriam Alexandre & Dr. Jonathan Cimino

TAKE HOME MESSAGE

1 **Clinical Research in Luxembourg is Changing**

2 **Centralized Management of National Clinical Trials by CIEC**

CIEC 10 years

CLINICAL AND EPIDEMIOLOGICAL INVESTIGATION CENTER

Excellence in clinical research

LUXEMBOURG INSTITUTE OF HEALTH

RESEARCH DEDICATED TO LIFE

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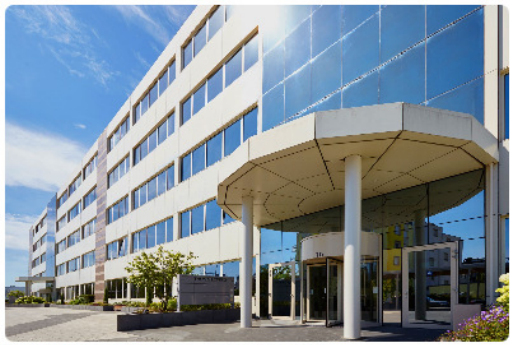
A few facts about LIH


HOUSE OF BIOHEALTH


LUXEMBOURG - EDISON


LUXEMBOURG - BAM

3
RESEARCH DEPARTMENTS

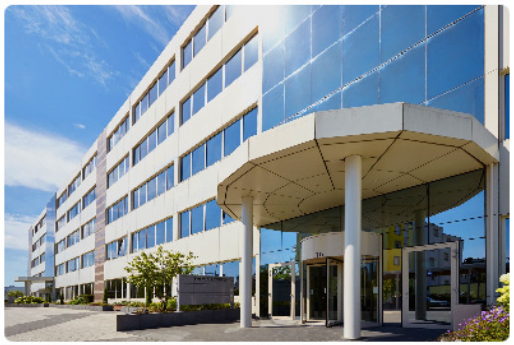
IBBL 1
BIOBANK

373
EMPLOYEES

35
NATIONALITIES

Luxembourg Institute of Health is a public biomedical research organization. Striving for excellence, its researchers, by their creativity, enthusiasm and commitment, generate knowledge on disease mechanisms and contribute to the development of new diagnostics, preventive strategies, innovative therapies and clinical applications that impact the healthcare of Luxembourgish and European citizens.

LUXEMBOURG INSTITUTE OF **HEALTH**
RESEARCH DEDICATED TO LIFE



LUXEMBOURG - EDISON

LIH EDISON BUILDING:

- Restricted and secured area
- Confidentiality guaranteed
- 7 dedicated consultation rooms
- Centrifuge, tensiometer, laminar flow hood…

10 CIEC years

CLINICAL AND EPIDEMIOLOGICAL INVESTIGATION CENTER

Excellence in clinical research

DEDICATED STAFF

Clinical Research Manager	Clinical Research Coordinator (2) / ECRIN EuCo *	Clinical Research Associate	Data Monitor	Research Nurse + Coordinator	Administrative Officer
Planning, implementation, and tracking of clinical trial activities Manage administration of clinical trials, maintaining an overview of the clinical trials (metrics & reporting, budget,…) Manage the team of study nurses and junior CRAs to conduct clinical trial and epidemiological studies	RA & CNER submissions Contracts & agreements Cost analysis & budget negotiations Resource allocation Study milestones follow-up Reporting ***EuCO** = European Correspondent	Establish & Follow-up SMF Set up of study documentation: CRF, ICF… Study initiation & on site visits Lead monitoring activities Ensure compliance with study protocol	Assist investigator & medical staff in study documentation & data entry & verification Collaborate with research nurses to ensure data monitoring activites & SDV	Assist investigator Monitor accuracy of data Follow-up of queries & safety data	Assist the research unit team in the overall performing a clinical research trial process Maintain clinical unit documentation (paper & electronic)

Flying Staff!

CIEC supporting functions (Quality, Legal, Finance, Tech & Security Management)
Competence Center in Methodology & Statistics (CCMS)

10 CIEC years

DEDICATED STAFF




4 CLINICAL RESEARCH ASSOCIATES


3 CLINICAL RESEARCH COORDINATORS









5 RESEARCH NURSES + COORDINATOR

2 ADMINISTRATIVE OFFICERS

2 DATA MONITORS


MISSIONS

PROVIDE

- Operational & educational support to hospitals and health care professionals
- Access to new and innovative therapeutic approaches/strategies for patients

PROTECT

- Patients' rights & safety
- Data privacy
- Good Clinical Practice (ICH-GCP).

ISO 9001 certification
GCP accreditation
Individual GCP certifications of CIEC staff (yearly update)
GDPR Compliant

PROMOTE

- Communication and valorization of Clinical Research
- Clinical Research according to Good Clinical Practice (ICH-GCP)
- Research integrity & ethics

PARTICIPATE

- Communication and valorization of Clinical Research
- Good Clinical Practice (ICH-GCP)
- Networks: ECRIN, EFGCP, ….

10 CIEC years

MISSIONS

PROVIDE

- Operational & educational support to hospitals and health care professionals
- Access to new and innovative therapeutic approaches/strategies for patients

MISSIONS

PROTECT

- Patients' rights & safety

- Data privacy, GDPR Compliant

- Good Clinical Practice (ICH-GCP).
  - In 10 years: from 0 to 36 procedures, templates & SOPs
  - GCP audit conducted in March 2018
  - Individual GCP certifications of CIEC staff (yearly update)

- ISO certification

CIEC 10 years

MISSIONS

PROMOTE

- **Communication and valorization of Clinical Research**
- Clinical Research according to Good Clinical Practice (ICH-GCP): yearly **GCP trainings for investigators** and staff
- Research integrity & ethics: provide **advice to researchers** in the conduct of clinical trials

LUXCLIN: UNIQUE PLATFORM DEDICATED TO CLINICAL RESEARCH IN LUXEMBOURG

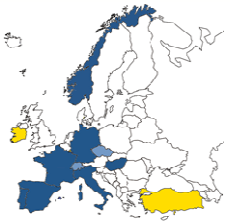
https://www.luxclin.lu/

MISSIONS

PARTICIPATE:
EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK (ECRIN)

Clinical Trials in Europe: CIEC contribution

ECRIN
EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK



ECRIN: European Clinical Research Infrastructure Network
= non-profit public research organisation

Aim: Support academic multinational clinical trials

- *Providing **information & consultancy**: logistical assessments, budget estimation, selection of sites, regulatory & ethics information in European countries*
- *Providing **services**: feasibilities, regulatory & ethics submissions, monitoring, project management, pharmacovigilance*
  - CIEC -> Luxembourg and Belgium
  - other ECRIN partners -> Germany, France, Italy, Spain, Portugal, Czech Republic, Norway…

Website: www.ecrin.org

Contact: Dr. Nancy De Bremaeker
Clinical Research Coordinator & ECRIN European correspondent

10 CIEC years

ACTIVITIES:

1 Observational
Healthy volunteers
Exploratory

2 Trials with IMP
Phase II & III
Registries

3 CTU for Belgium & Luxembourg
Coordination of EU trials

CIEC

STRASSEN – r. Thomas Edison

EHES Measuring the Health of Europeans

EpiPath

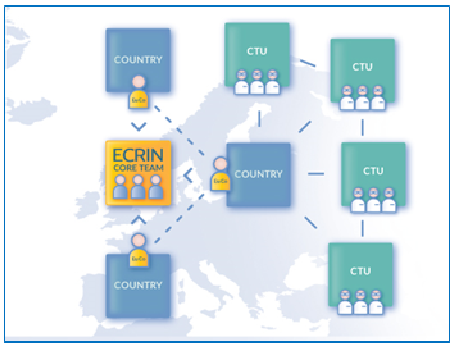
ORISCAV-LUX

PARKINSON National Centre of Excellence in Research

CHL Centre Hospitalier de Luxembourg

LUXEMBOURG – CHL

PHARMA



ECRIN
EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

VISION-DMD

ReveraGen BioPharma

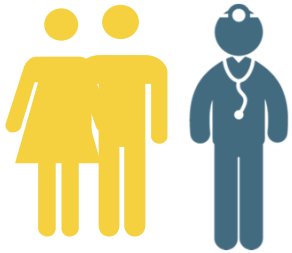
European Commission

10 CIEC years

CLINICAL RESEARCH EXPERTISE: FROM RESEARCH TO CLINIC

FROM RESEARCH

CIEC + CCMS



TO CLINIC

Patient oriented

Investigator Support

Clinical project management

National & International Network
Partnerships with Healthcare institutions

Secured infrastructures
and equipements

Qualified staff - GCP compliant

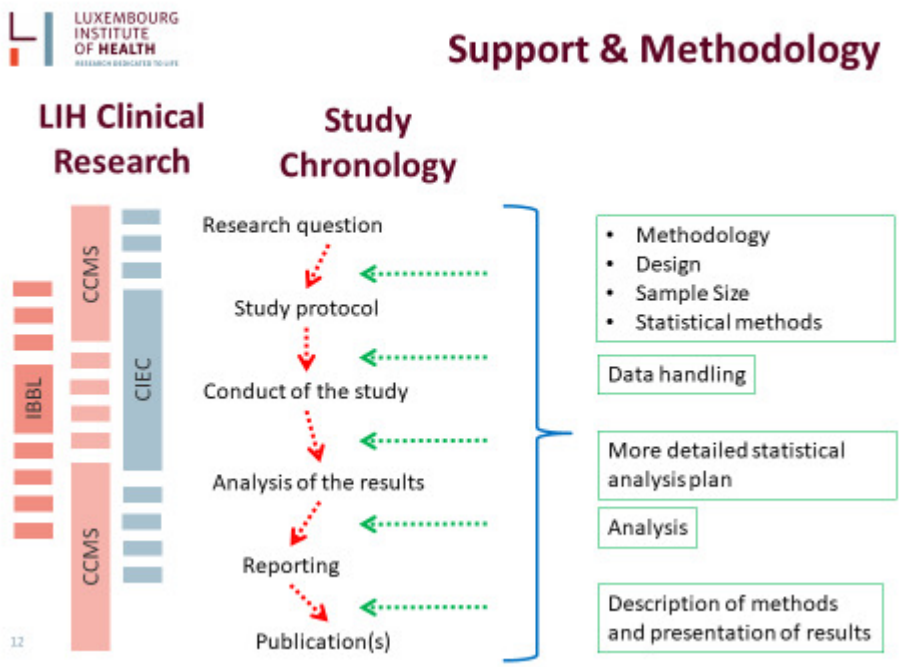
Competence Center for Methodology and Statistics CCMS: Complementary to CIEC

Design and planning before protocol writing

Case report form (to collect data) adapted to IT system

Follow-up of data collection and monitoring of the study

Documentati



CLINICAL BOX: FROM DESIGN TO PUBLICATION

Project

+ CCMS

- Research Idea
- Project planning
- Funding solutions

1-6 M

Start-up phase

+ CCMS

- Essential documents writing (protocol, ICF,…)
- Regulatory submissions
- Contract Management
- Study set-up and collaboration with other dept.: pharmacy, laboratory, radiology, cardiology…
- Initiation visits
- Investigator trainings
- Work document development

3-6 M

Clinical phase

+ CCMS

- Recruitment/Visibility
- Screening activities on-site
- Inform consent process
- Medical assessments
- IVRS management
- Drug management
- Sample management
- Patient Visit calendar Protocol explanations
- SAEs/AEs follow up

1-2 Y

Follow-up

+ CCMS

- Data collection : Data management
- Assisting sponsor's monitoring visits
- Investigator site file management
- Invoicing,
- Closing activities and archiving

1-2 Y

Closing phase

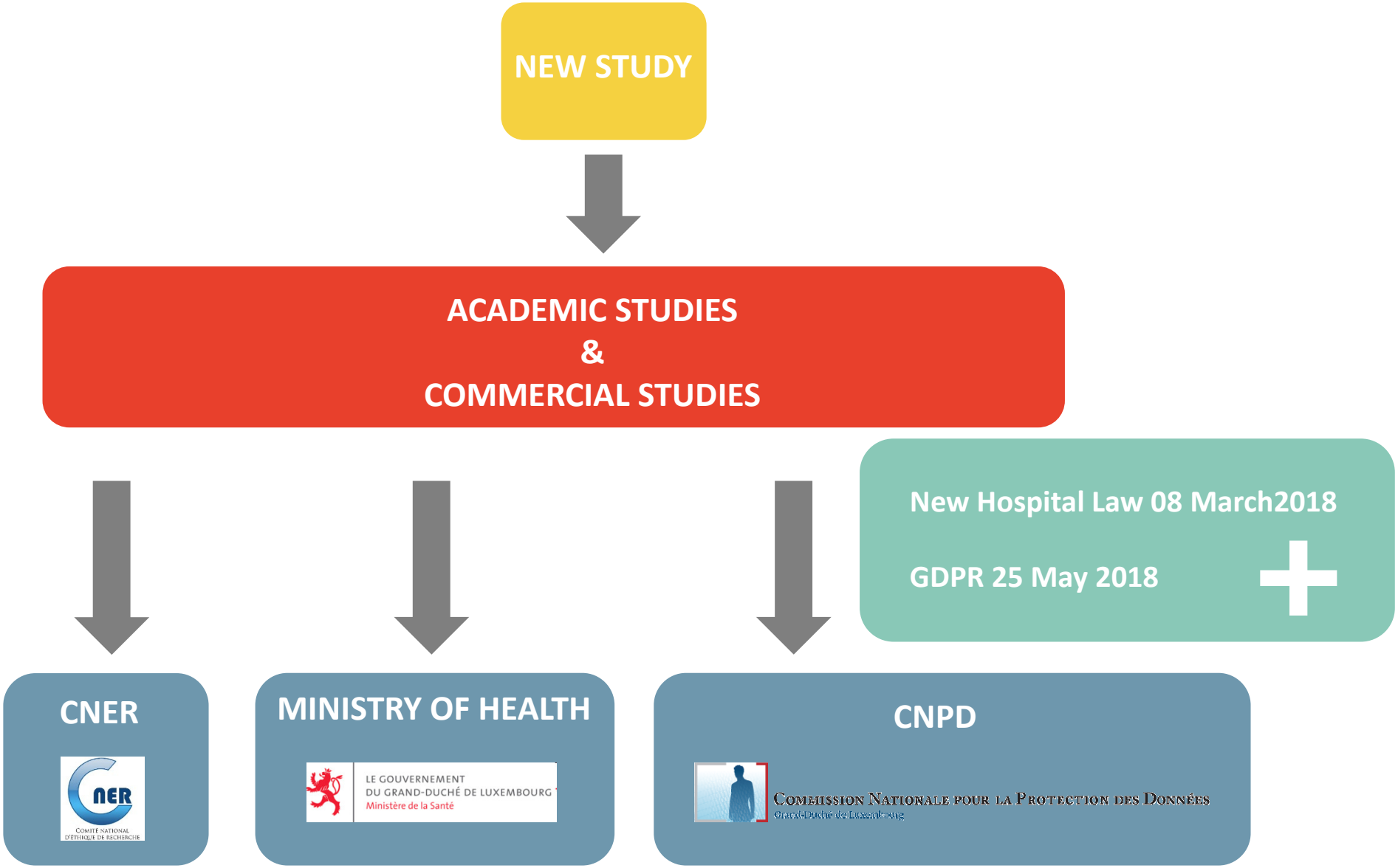
+ CCMS

- Data Base Management
- Statistical analysis
- Final report
- Publication of results
- Presentation of results

2-6 M

10 CIEC years

REGULATORY AND ETHICS SUBMISSIONS



CLINICAL BOX: FROM DESIGN TO PUBLICATION

Project

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- Research Idea
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1-6 M

Start-up phase

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3-6 M

Clinical phase

+ CCMS

- Recruitment/Visibility
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1-2 Y

Follow-up

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- Closing activities and archiving

1-2 Y

Closing phase

+ CCMS

- Data Base Management
- Statistical analysis
- Final report
- Publication of results
- Presentation of results

2-6 M

10 CIEC years

OVER 10 YEARS

+140
STUDIES

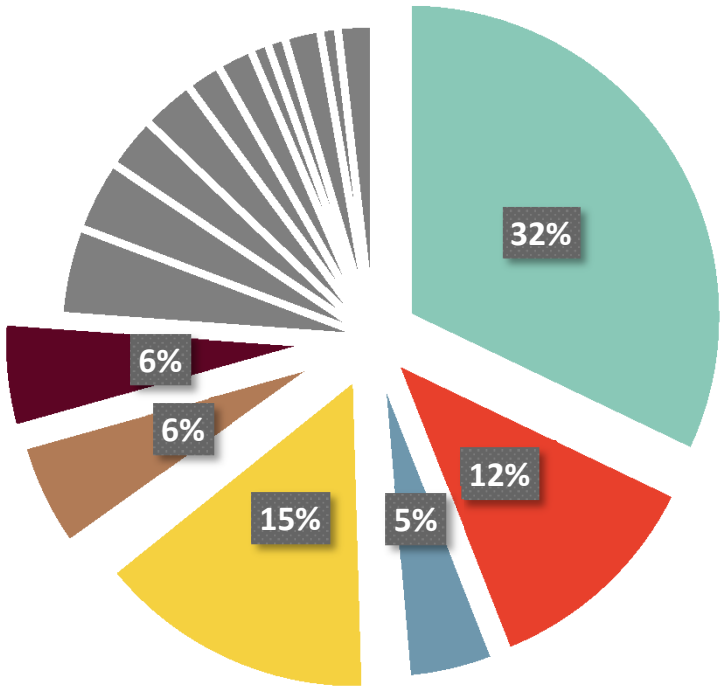
+80
INVESTIGATORS
INVOLVED

+7000
PARTICIPANTS
INCLUDED

+60
SPONSOR
COLLABORATION

10 CIEC years

THERAPEUTIC AREAS AND EXPERIENCE



- Oncology
- Hemato
- CUP Onco
- Infectious Diseases
- Pulmology
- Coll. IBBL
- LNSI
- Coll. ECRIN
- Neuro surgery (pain therapy)
- Nutrition
- Primary Care
- Orthopedics
- Other: Abdominal surgery
- Neurology
- Diabetes
- Cardiovascular
- Immuno/Allergy

CIEC 10 years

NATIONAL & INTERNATIONAL KEY ACTORS

NETWORKS

- ECRIN
- EUPATI
- EFGCP
- EUSTM
- WIN

REGULATORY AUTHORITIES

- Ministry of Health
- Ministry of Research
- CNER
- CNPD

HEALTHCARE INSTITUTIONS / CENTERS

- CHL
- CHEM
- Hôpitaux Robert Schuman
- CHdN
- General Practitoner's
- Dieticians
- . . .

RESEARCH INSTITUTIONS

- Luxembourg Institute of Science and Technology
- Laboratoire National de la Santé
- IBBL
- University of Luxembourg / Brussels
- Hovon, Netherlands
- Breast Internaltional Group
- Centre François Baclesse
- Institut Bordet, Brussels
- . . .

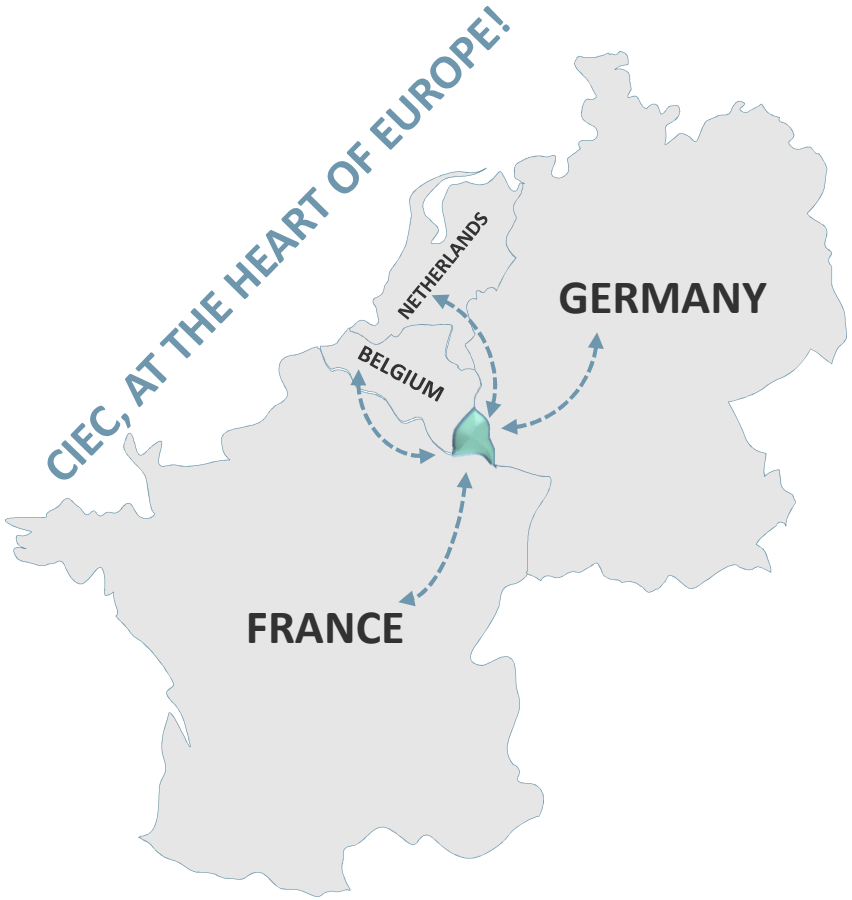
PHARMACEUTICAL COMPANIES

- More than **25** partners

CLINICAL RESEARCH ORGANIZATION

10 CIEC years

OPEN FOR CLINICAL COMMUNITY?



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