Innovative models in biomedical research

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95% rats & mice

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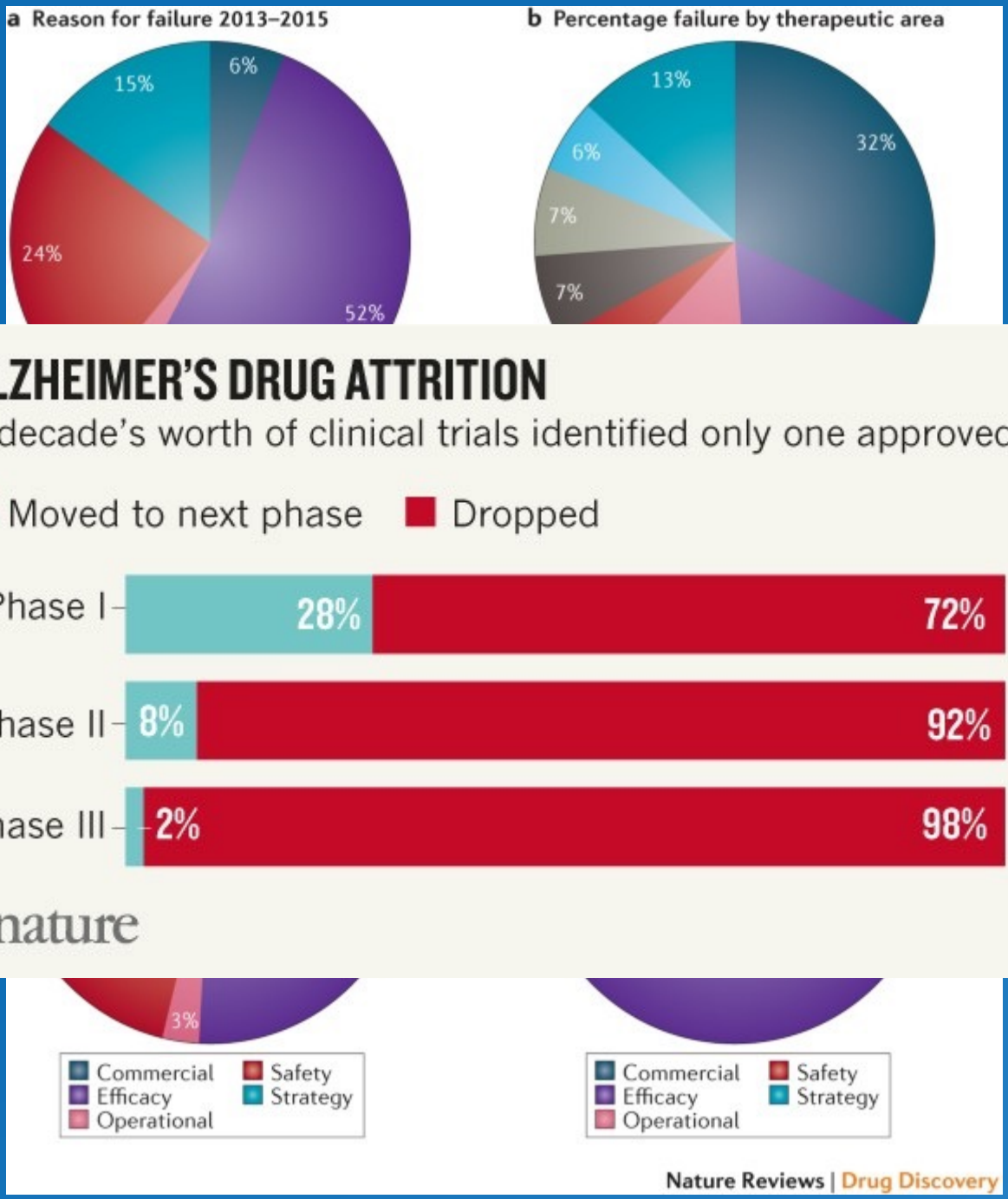

ALZHEIMER'S DRUG ATTRITION

A decade's worth of clinical trials identified only one approved drug.

Moved to next phase Dropped

	Moved to next phase	Dropped
Phase I	28%	72%
Phase II	8%	92%
Phase III	2%	98%

99.6% of **413** trials (testing a total of **244** compounds from 2002 to 2012) failed to produce a drug.

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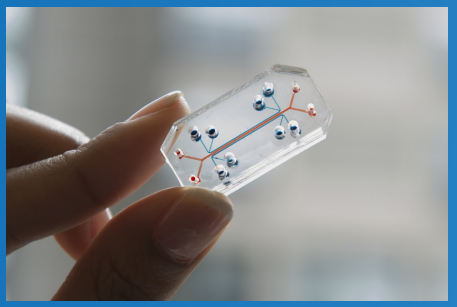
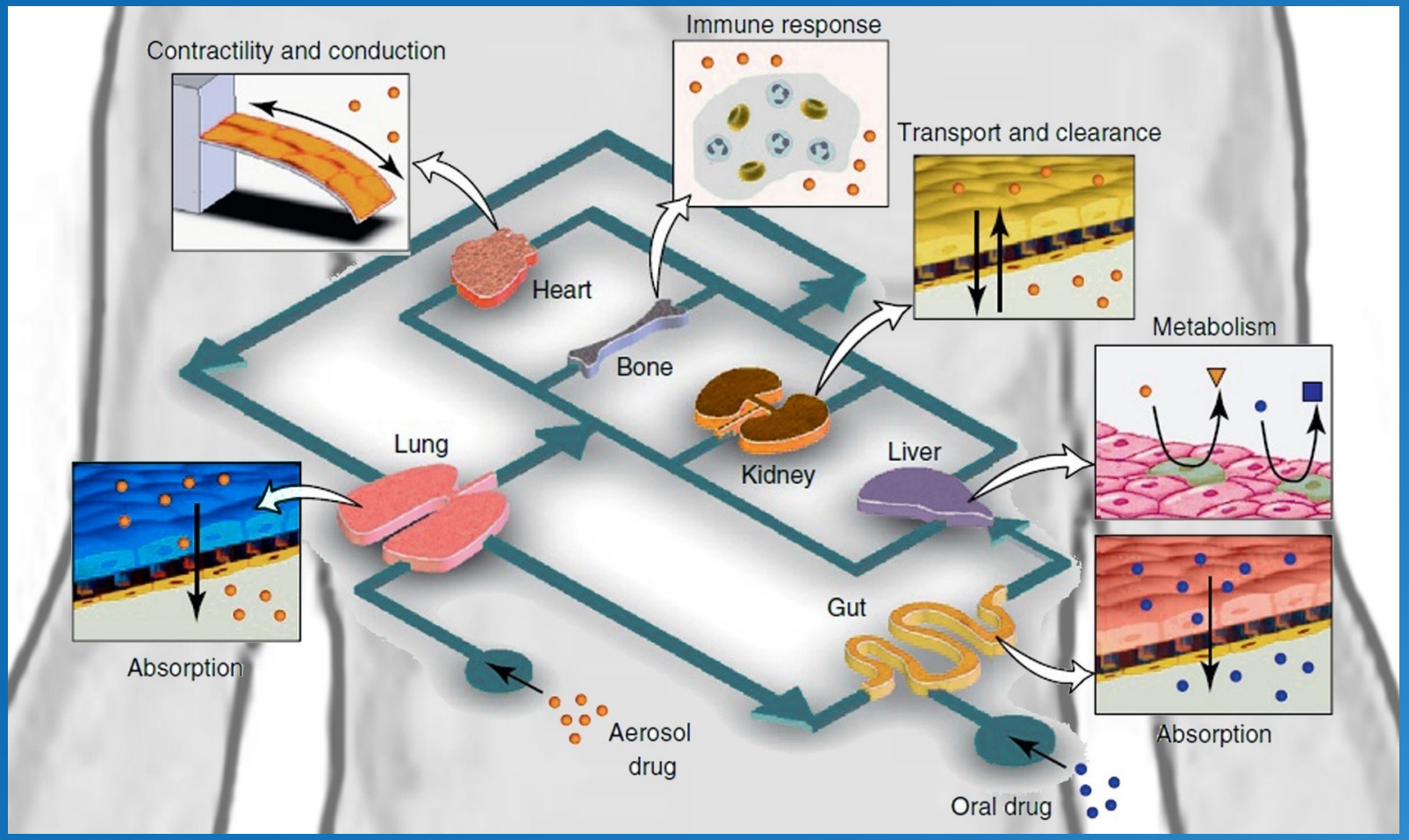
Innovative NAMs





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Non-animal methods used in research

- **Knowledge-base** of models
- **Meta-analyses** to understand strategies and approaches

Respiratory tract diseases

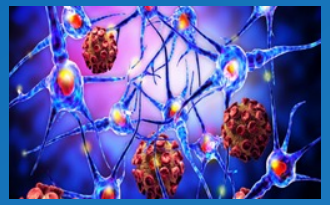
Neurodegenerative diseases

Cardiovascular diseases

Breast Cancer

Immunogenicity testing for ATMPs

Immuno-oncology



Autoimmune diseases

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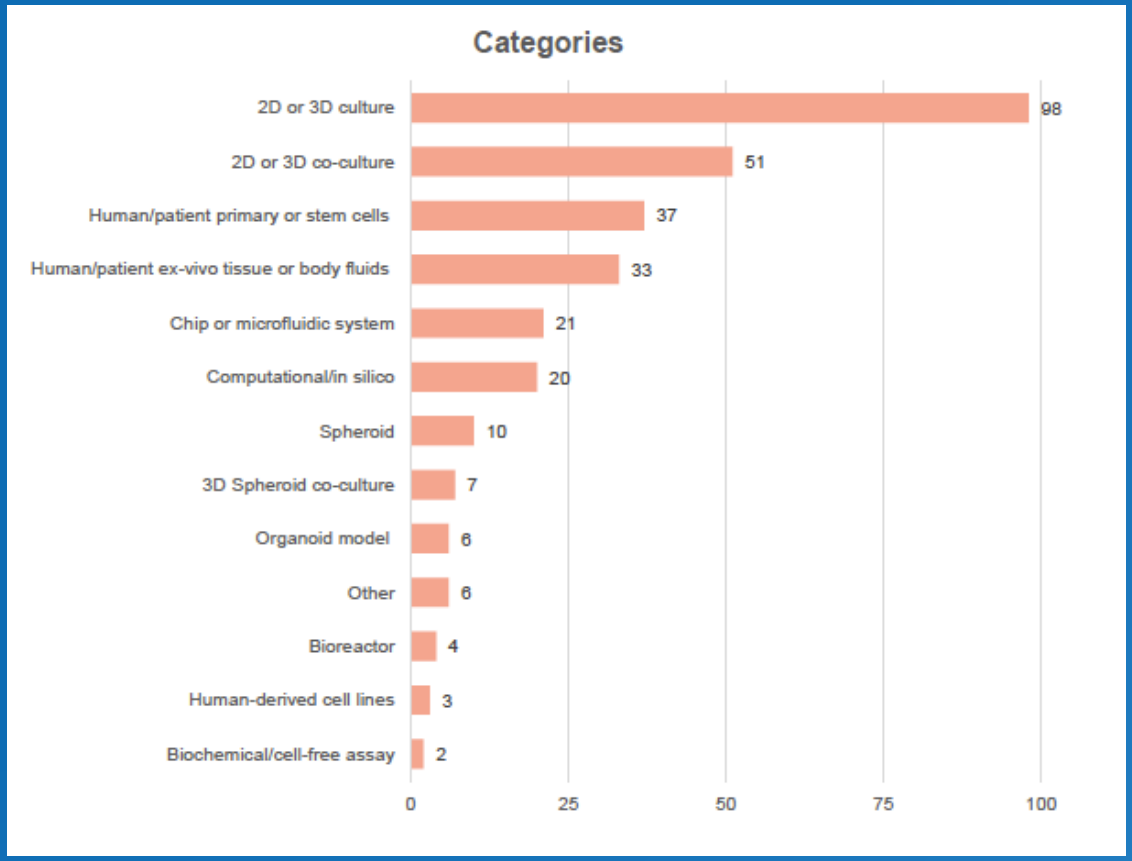
Respiratory Tract Diseases



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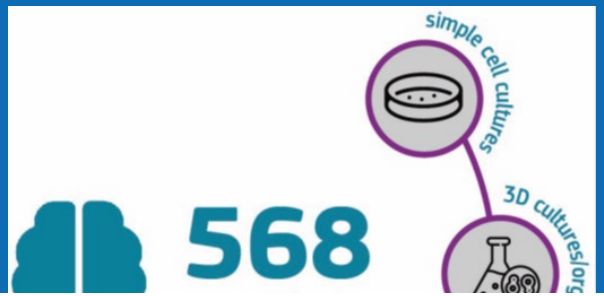
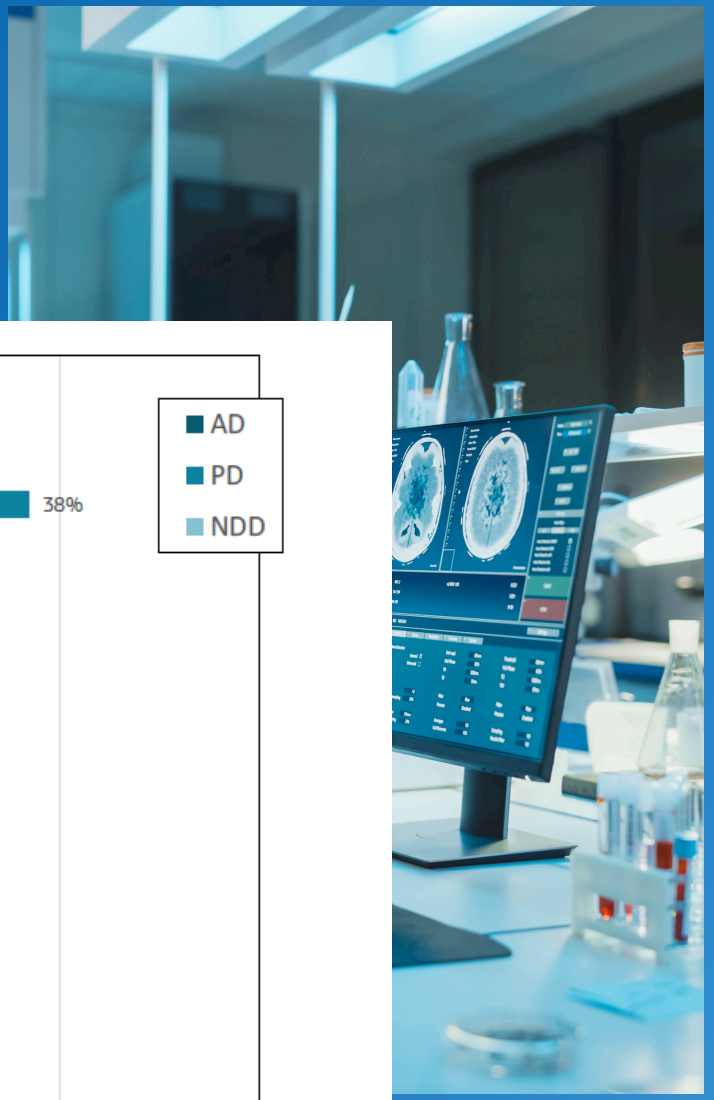
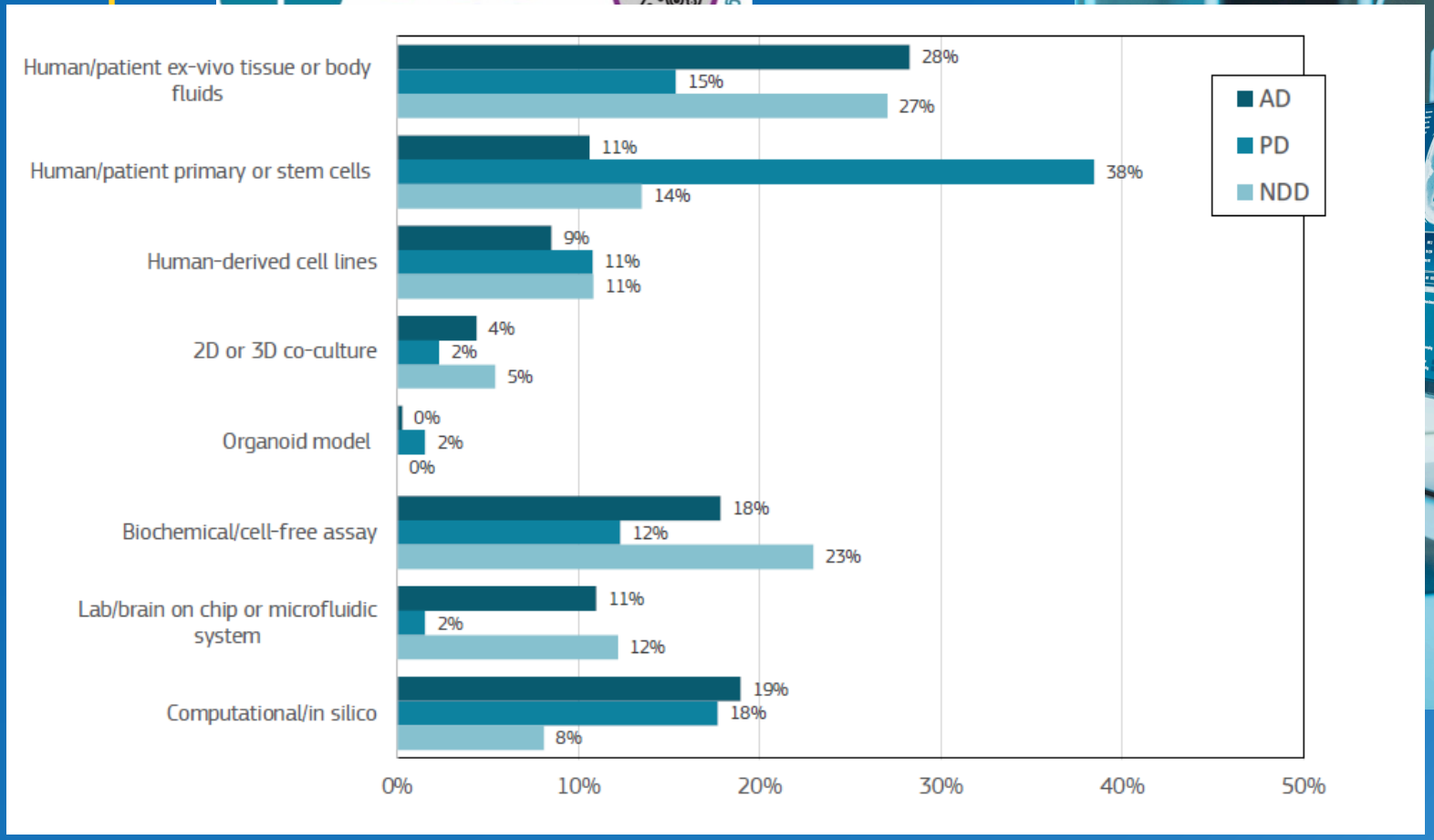
Neurodegenerative disease







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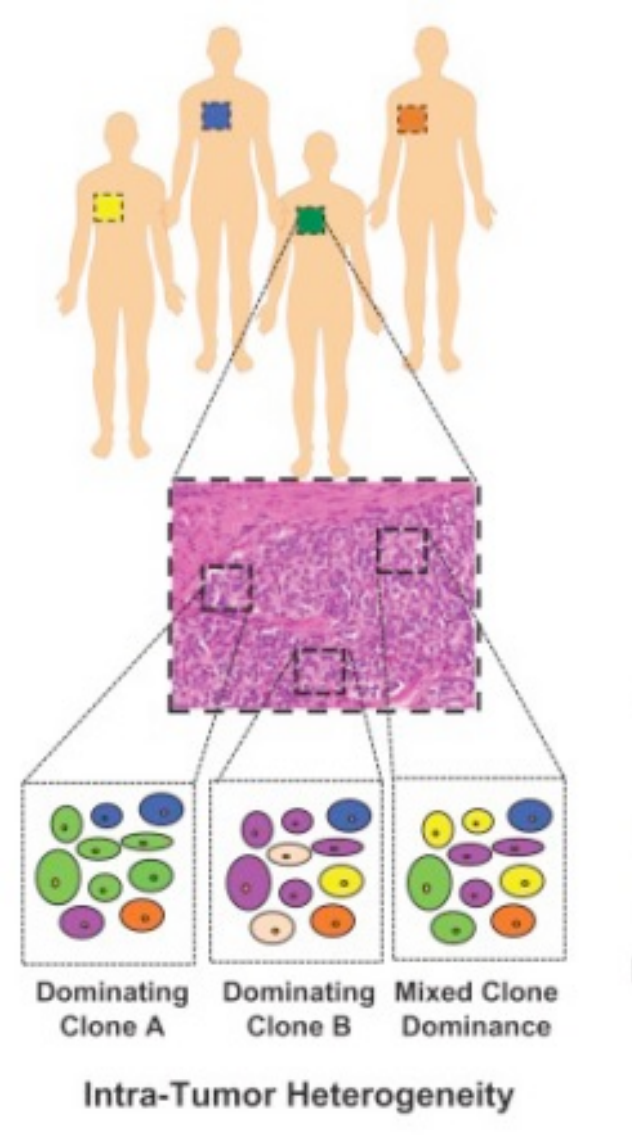
Breast Ca



In EU over 355,000 women diagnosed with breast cancer in 2020 (source: ECIS)

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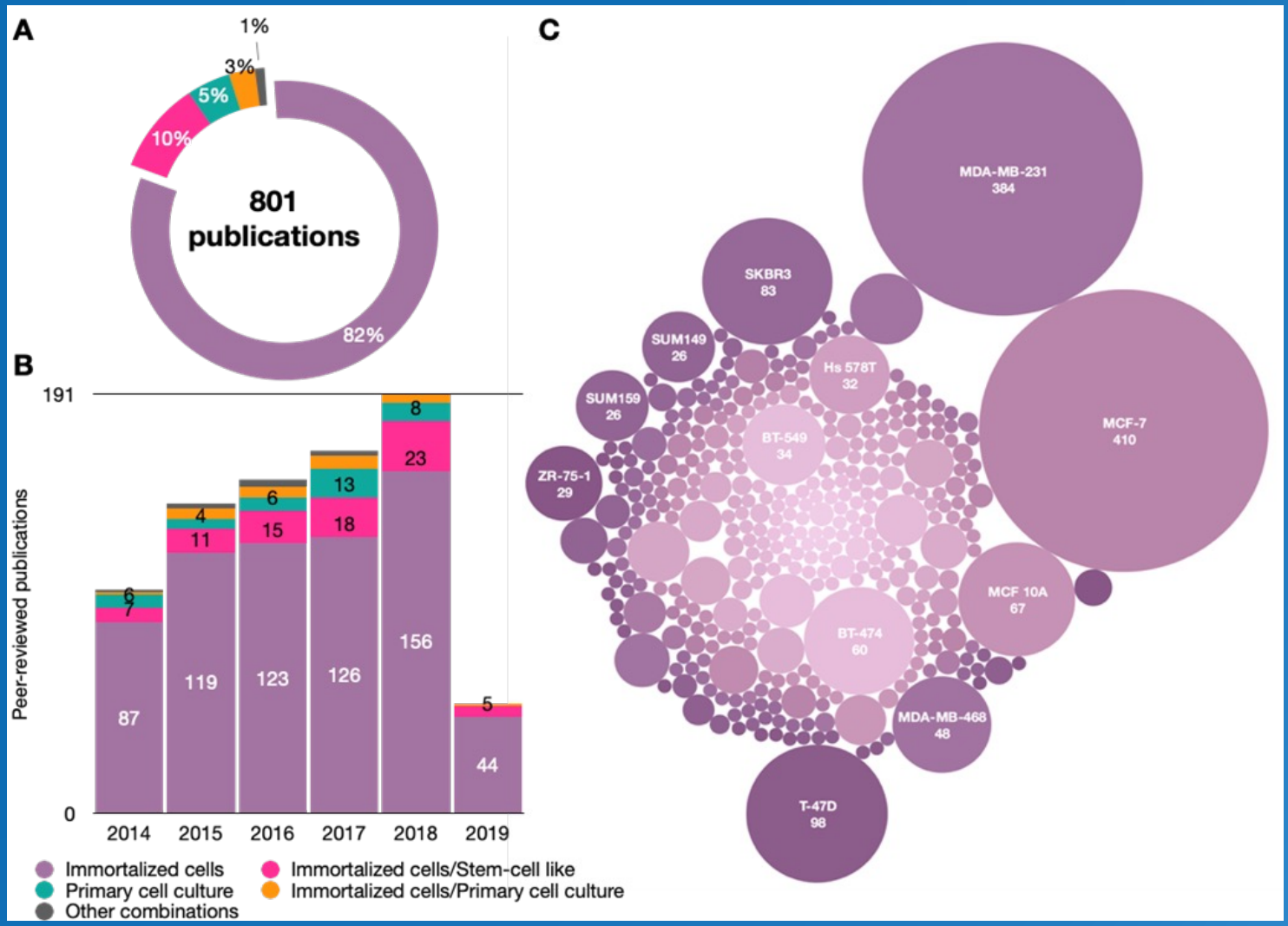

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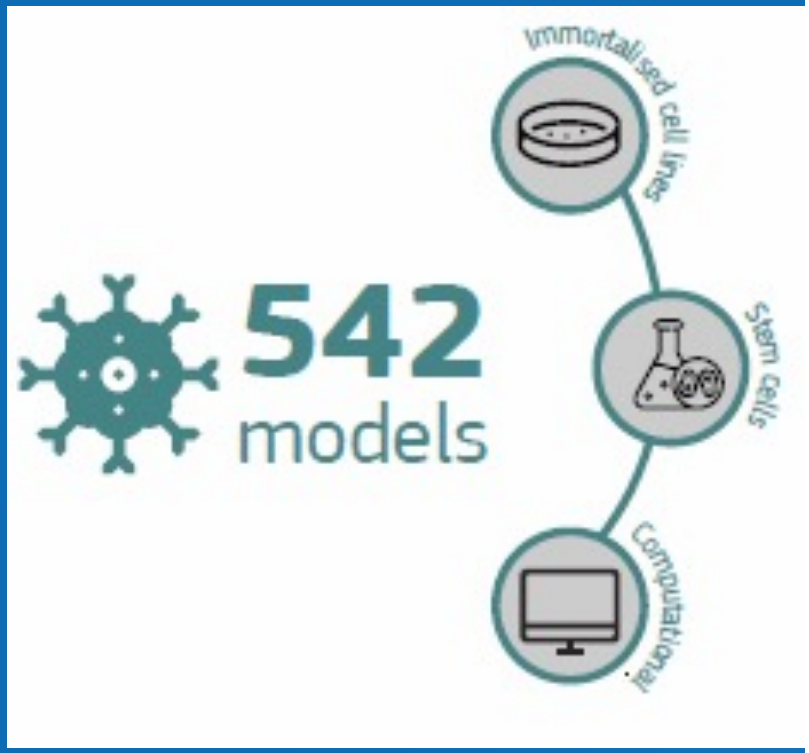
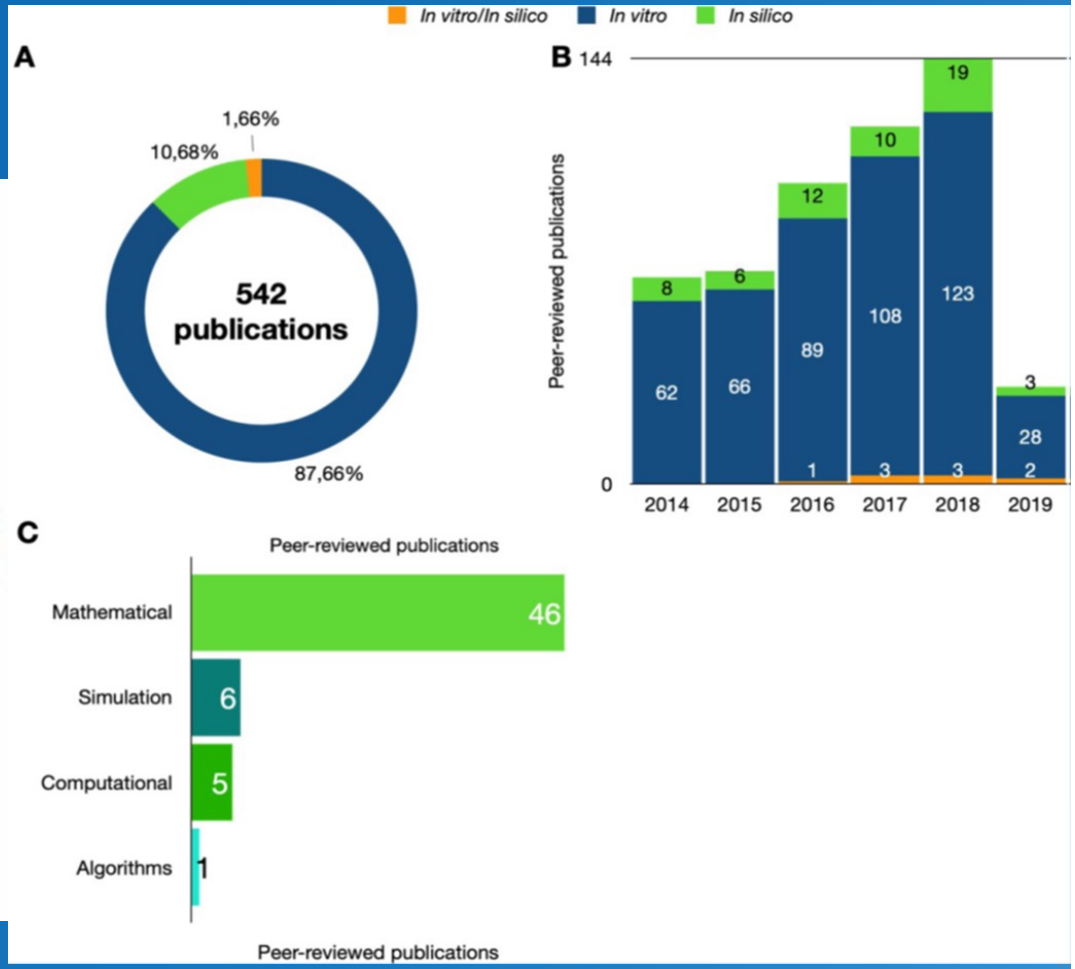
Immuno-oncology





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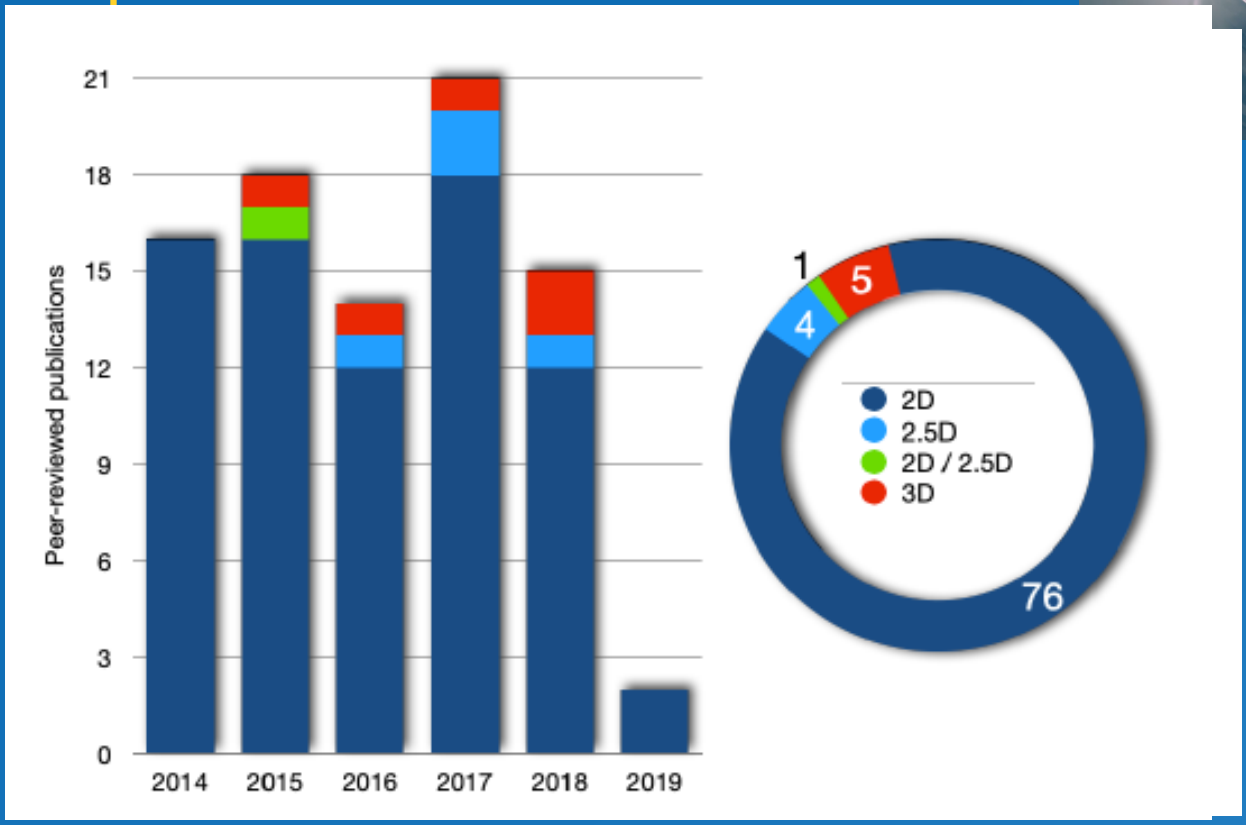
Immunogenicity for ATMP testing



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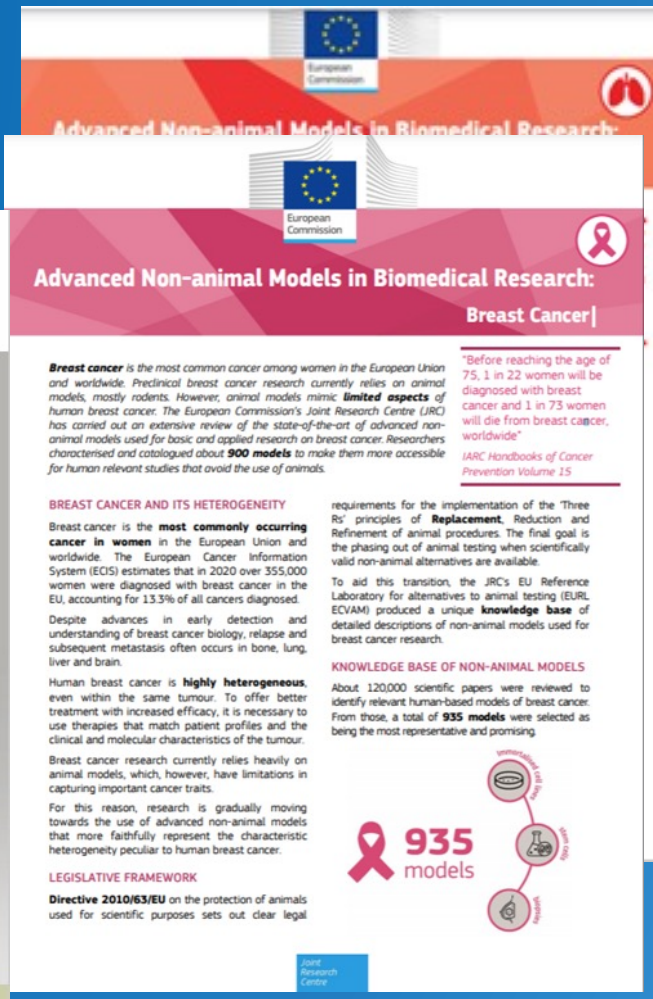

- **Technical Report**
- **Executive Summary**
- **Leaflets**
- **JRC Data catalogue**

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A	B	C	D	E	F	G	H	I	J	K	L	M
Model no.	Disease area	Disease feature	Category	Type	Application/ aim	Biological or disease-specific endpoint	Assay Throughput/ Content	Relevance	Potential/Future developments	DOI	Author name	Year
1	AD	Protein aggregation	Lab/brain on chip or microfluidic system	Proteins	Disease mechanism (exp/theor)	Protein dysfunction: amyloid peptide (any version)	Low-medium/medium	Medium - Attempting to recapitulate fluid-	A more complete in vitro microfluidic system for studying	http://dx.doi.org/10.1021/acschemneuro.7b00285	Gospodarczyk	2017
2	AD	Protein aggregation	Lab/brain on chip or microfluidic system	Proteins	Drug developm/ testing	Protein dysfunction: BACE1	High (automatic)/low	Low - Method of screening therapeutics, BACE1	Could be applied to additional small molecule libraries	http://dx.doi.org/10.1007/s00216-017-0617-y	Liu	2017
3	AD	Protein aggregation	Lab/brain on chip or microfluidic system	Proteins	Diagnosis of disease	Protein dysfunction: amyloid peptide (any version)	High (automatic)/low	Low - Diagnosis of disease by detection of	The high sensitivty of the device suggests that it may	http://dx.doi.org/10.1038/s41598-017-14338-4	Yoo	2017
4	AD	Protein aggregation	Lab/brain on chip or microfluidic system	Proteins	Drug developm/ testing	Protein dysfunction: BACE1	High (automatic)/low	Low - Method of screening therapeutics, BACE1	Could be integrated into fully automated system	http://dx.doi.org/10.1016/j.chroma.2017.08.065	Roman	2017
5	AD	Protein aggregation	Lab/brain on chip or microfluidic system	Proteins	Diagnosis of disease	Protein dysfunction: amyloid peptide (any version)	High (automatic)/low	*Low - Diagnosis of disease by detection of Amyloid Beta,*	May be adapted to detection of other biomarkers	http://dx.doi.org/10.3390/bios7030029	Dai	2017
6	AD	Neuroinflammation	2D or 3D co-culture	Neurospheres/3D model	Drug developm/ testing	Changed protein expression	High (automatic)/medium	High - throughput of 96well compatible format >1000	Model likely to be used for high throughput drug	http://dx.doi.org/10.1038/s41598-018-20436-8	Jorfi	2018
7	AD	Protein aggregation	Lab/brain on chip or microfluidic system	Proteins	Diagnosis of disease	Protein dysfunction: amyloid peptide (any version)	High (automatic)/low	Low - Diagnosis of disease by detection of	Magnetic Bead assay could automated for high	http://dx.doi.org/10.1016/j.snb.2017.09.003	Mai	2018
8	AD	Protein aggregation	Lab/brain on chip or microfluidic system	Proteins	Diagnosis of disease	Protein dysfunction: amyloid peptide (any version)	High (automatic)/low	Low - Diagnosis of disease by detection of	Magnetic Bead assay could automated for high	http://dx.doi.org/10.1016/j.bios.2014.10.042	Kim	2015
9	AD	Protein aggregation	Lab/brain on chip or microfluidic system	Proteins	Disease mechanism (exp/theor)	Protein dysfunction: amyloid peptide (any version)	High (automatic)/medium	Medium - Platform for studying in vitro protein-protein	Can be used for a variety of proteins and determination	http://dx.doi.org/10.1016/j.bios.2014.11.025	Wang	2015
10	Several NDD	Exploratory/ no specific feature	Biochemical/cell-free assay	Fibrils	Disease mechanism (exp/theor)	Protein dysfunction: a-synuclein	Low-medium/low	Medium - Platform for fibril growth (PD-related)	Could be used for identification of compunds that	http://dx.doi.org/10.1016/j.jmb.2015.01.020	Woerdehoff	2015
11	PD	Neuroinflammation	Lab/brain on chip or microfluidic system	Co-culture model (multiple cells)	Disease mechanism (exp/theor)	Oxidative/nitrosative stress	High (automatic)/medium	Medium - In vitro platform for investigation of	Could be used to study generation of chemotaxis	http://dx.doi.org/10.3389/fnins.2016.00511	Fernandes	2016
12	PD	Protein aggregation	Lab/brain on chip or microfluidic system	Co-culture model (multiple cells)	Disease mechanism (exp/theor)	Protein dysfunction: a-synuclein	High (automatic)/medium	Medium - In vitro platform for investigation of a-	Could be used to study generation of chemotaxis	http://dx.doi.org/10.3389/fnins.2016.00512	Fernandes	2017
13	Several NDD	Exploratory/ no specific feature	Lab/brain on chip or microfluidic system	Other	Disease mechanism (exp/theor)	Mitochondrial dysfunction	High (automatic)/medium	Medium - In vitro platform for measuring	Could be applied to specific disease-state models as a	http://dx.doi.org/10.1007/s13238-016-0268-3	Chen	2016
14	AD	Protein aggregation	Lab/brain on chip or microfluidic system	Proteins	Diagnosis of disease	Protein dysfunction: amyloid peptide (any version)	High (automatic)/low	Low - SPR platform used for measuring amyloid beta	High sensitivity suggests could be used for clinical	http://dx.doi.org/10.3938/jkps.69.793	Kim	2016
15	AD	Protein aggregation	Lab/brain on chip or microfluidic system	Peptides	Disease mechanism (exp/theor)	Protein dysfunction: amyloid peptide (any version)	High (automatic)/low	Medium - In vitro platform for measuring APP	Could be used to investigate neurite specific response to	http://dx.doi.org/10.1002/adhm.201600895	Li	2017

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Main Conclusions

- Extensive use of NAMs (esp. *in vitro*) but clear need for more complex ones.
- Standard operating procedures (SOP) for model generation and testing will be essential and should be encouraged.
- Promote more effective cross-talk and multidisciplinarity between different fields - essential for further development of organoid, OoC etc models.

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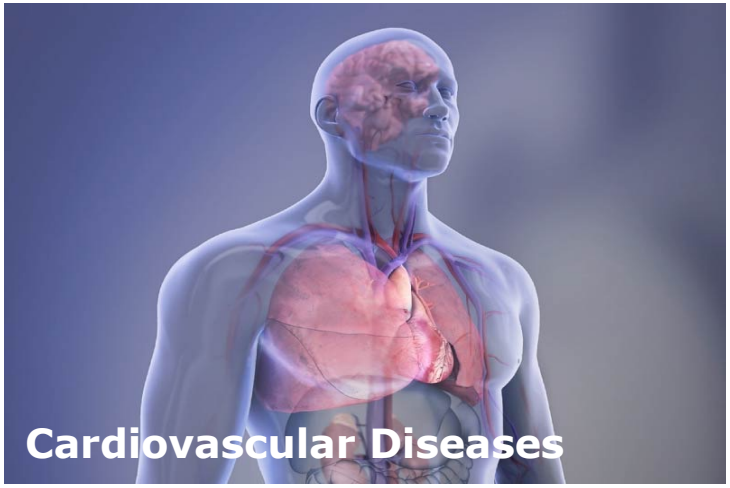
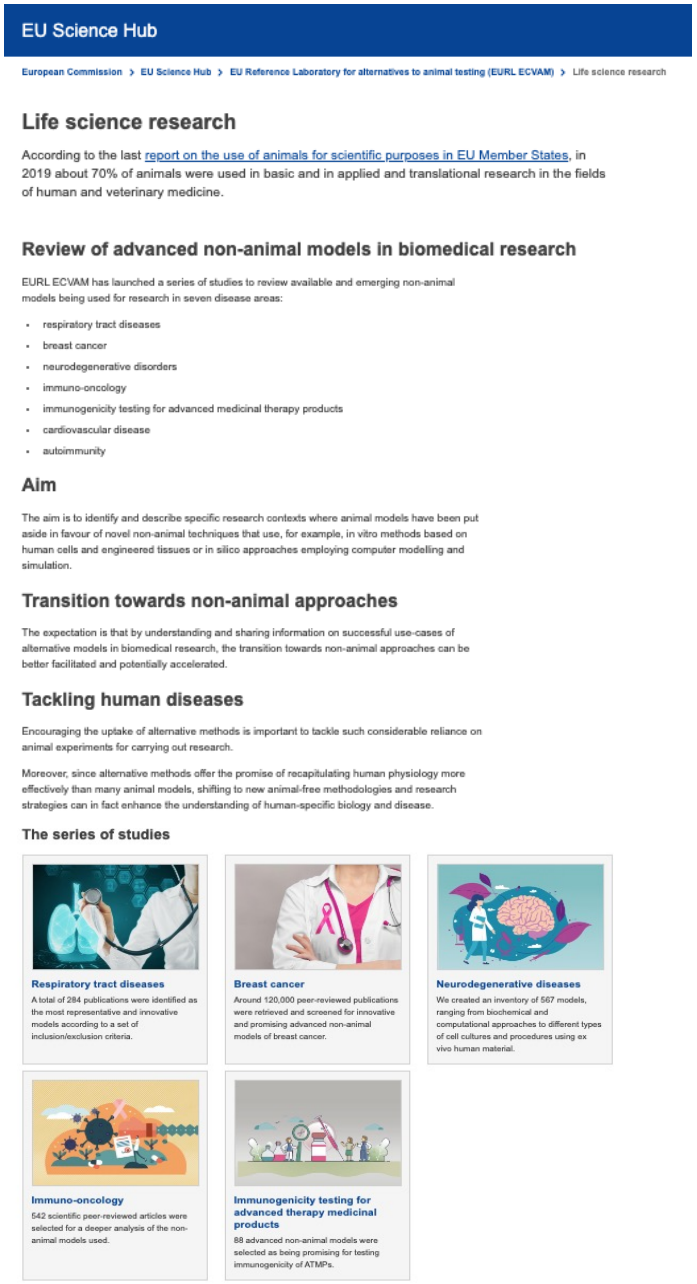
Dissemination Plan

- Research groups submitting a project proposal which makes use of living animals;
- Animal Welfare Bodies advising research groups on project proposals;
- Competent Authorities who are responsible for project evaluation;
- National Committees that facilitate a coherent approach to project evaluation, dissemination of information and sharing of best practice within each Member State;
- National Contact Points, who are responsible for the implementation of the Directive in the Member States

Coming Soon





EU Science Hub

European Commission › EU Science Hub › EU Reference Laboratory for alternatives to animal testing (EURL ECVAM) › Life science research

Life science research

According to the last report on the use of animals for scientific purposes in EU Member States, in 2019 about 70% of animals were used in basic and in applied and translational research in the fields of human and veterinary medicine.

Review of advanced non-animal models in biomedical research

EURL ECVAM has launched a series of studies to review available and emerging non-animal models being used for research in seven disease areas:

- respiratory tract diseases
- breast cancer
- neurodegenerative disorders
- immuno-oncology
- immunogenicity testing for advanced medicinal therapy products
- cardiovascular disease
- autoimmunity

Aim

The aim is to identify and describe specific research contexts where animal models have been put aside in favour of novel non-animal techniques that use, for example, in vitro methods based on human cells and engineered tissues or in silico approaches employing computer modelling and simulation.

Transition towards non-animal approaches

The expectation is that by understanding and sharing information on successful use-cases of alternative models in biomedical research, the transition towards non-animal approaches can be better facilitated and potentially accelerated.

Tackling human diseases

Encouraging the uptake of alternative methods is important to tackle such considerable reliance on animal experiments for carrying out research.

Moreover, since alternative methods offer the promise of recapitulating human physiology more effectively than many animal models, shifting to new animal-free methodologies and research strategies can in fact enhance the understanding of human-specific biology and disease.

The series of studies

Respiratory tract diseases
A total of 284 publications were identified as the most representative and innovative models according to a set of inclusion/exclusion criteria.

Breast cancer
Around 120,000 peer-reviewed publications were retrieved and screened for innovative and promising advanced non-animal models of breast cancer.

Neurodegenerative diseases
We created an inventory of 567 models, ranging from biochemical and computational approaches to different types of cell cultures and procedures using ex vivo human material.

Immuno-oncology
542 scientific peer-reviewed articles were selected for a deeper analysis of the non-animal models used.

Immunogenicity testing for advanced therapy medicinal products
88 advanced non-animal models were selected as being promising for testing immunogenicity of ATMPs.

https://joint-research-centre.ec.europa.eu/eu-reference-laboratory-alternatives-animal-testing/knowledge-sharing-three-rs/life-science-research_en

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Work in progress

- This year, the EP funded a Pilot Project to develop an automated database to collect and structure NAMs for use in biomed research.
- Based on this dataset for training machine learning algorithms or AI.
- We are launching the project with the aim to complete it by 2024 when a consolidated version of the dataset should be published.

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Thank you!

Views expressed in this presentation are the ones of the presenter and do not necessarilly reflect the official views of the European Commission.

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