Centro 3R

Ferdinando Chiaradonna

Università degli Studi di Milano Bicocca

Dipartimento di Biotecnologie e Bioscienze

Biologia cellulare

Modelli in silico

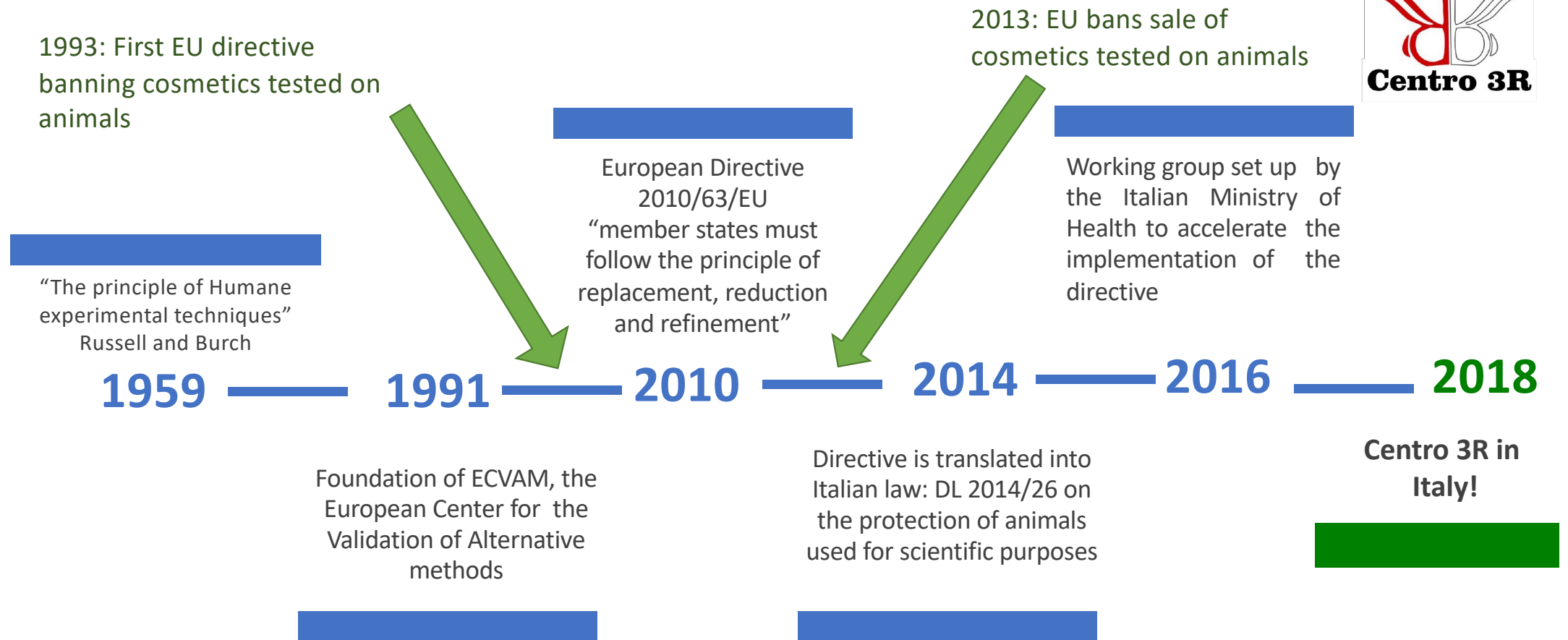Modelli in vitro

3Rs principles

The 3Rs stand for **Replace**, **Reduce**, **Refine** and represent a responsible approach to animal testing.

The goal is
to **replace animal experiments whenever possible**

to keep the number of animal experiments as low as possible

to only **use the necessary number of animals**

- 3R TIMELINE IN EUROPE & ITALY

1993: First EU directive banning cosmetics tested on animals

2013: EU bans sale of cosmetics tested on animals

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"The principle of Humane experimental techniques" Russell and Burch

European Directive 2010/63/EU "member states must follow the principle of replacement, reduction and refinement"

Working group set up by the Italian Ministry of Health to accelerate the implementation of the directive

1959 —— **1991** —— **2010** —— **2014** —— **2016** —— **2018**

Foundation of ECVAM, the European Center for the Validation of Alternative methods

Directive is translated into Italian law: DL 2014/26 on the protection of animals used for scientific purposes

Centro 3R in Italy!

Interuniversity Center for the Promotion of the 3Rs Principles in Teaching and Research
CENTRO 3R

Vision: an interuniversity infrastructure for guiding the implementation and integration of the 3Rs in scientific curricula and in basic and applied research

Mission: promote humane and evidence-based thinking through education and research *for the mutual benefit of humans, animals and the environment* (ONE HEALTH)

Strategy: sharing teaching and learning methodologies and resources.

3Rs=better science

PREMISES

- The EU directive 2010/63 acknowledges that encouraging the application of 3Rs principles requires teaching and dissemination

- Concept of 3Rs not well known

- A bottom up approach, addressing the grass roots of scientific culture is needed

- Universities are the primary venue for free teaching and free research

- Ergo, Universities are the ideal ground for promoting methods which respect the 3Rs in basic and translational research

- <u>First draft , November 2016</u>

- <u>The Center was formally set up in January 2018 after approval from the Senate and Admin Councils of University of Pisa and University of Genova.</u>

MAIN OBJECTIVES

a) Promote the establishment of courses focused on the 3Rs within the core curricula of scientific degree programs.

b) Create a multidisciplinary open e-infrastructure with:

- Teaching resources to facilitate the teaching of 3Rs principles;

- News and links for researchers to find resources which may be useful for 3Rs;

- An internal platform for sharing animal tissues;

- An instrument for rehabilitating lab animals.

OTHER OBJECTIVES

c. Promote scientific and cultural debates;

d. Promote, develop and coordinate interdisciplinary studies in the context of the 3Rs;

e. Implement, promote, develop and use new integrated in-silico and in-vitro methods;

f. Organize courses, seminars, refresher courses and meetings within various scientific disciplines.

g. Establish prizes, fellowships for young researchers to encourage 3Rs studies;

h. Encourage collaboration with the *Organismi Preposti al Benessere Animale* to favour the adoption of alternative methods;

i. Encourage technology transfer and translational research;

j. Encourage national and international collaboration.

MULTIDISCIPLINARY COMPETENCIES

BIOLOGY

COMPUTATIONAL MODELS

AWBs

BIOMATERIALS, BIOREACTORS & BIOFABRICATION

REGULATION/ LAW /ETHICS

TOXICOLOGY

PHARMACOLOGY

PATHOLOGY

VETERINARY SCIENCE

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THE BOARD

Centro 3R

DIRECTOR	Vice-DIRECTOR

CONSIGLIO
SCIENTIFICO-DIDATTICO
(CSD)

UNITA' OPERATIVA
1

UNITA' OPERATIVA
2

UNITA' OPERATIVA
3

UNITA' OPERATIVA
N

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Achievements

- FROM 2 TO 11 UNIVERSITIES IN 6 YEARS
- OVER 350 MEMBERS
- EXPERT MEMBER OF THE NATIONAL COORDINATION GROUP ON WELFARE OF LAB ANIMALS
- COORDINATION BETWEEN THE NATIONAL CENTER OF REFERENCE/CENTRO 3R/PARERE
- MEMBER OF EU3RNET

Centro 3R

Teaching

NEW COURSES IN DEGREE and POST DOCTORAL PROGRAMS
- PHARMACY
- BIOLOGY
- BIOMEDICAL ENGINEERING
- VETERINARY SCIENCE- FELASA ACCREDITED
- MEDICINE

Still to be done

- FUNDING
- ADDING GOOD PRACTICE IN EXPERIMENTAL SCIENCE AND USE OF 3Rs AS A CORE SKILL IN CURRICULA DESCRIPTORS
- INVOLVING UNIVERSITIES IN SOUTHERN ITALY

Concrete strategies

Dissemination through website and social media platforms

Courses

Support in creating courses on the 3Rs

Centro 3R congress

Participation in EU 3R networks

Between the lines

- **3Rs is inclusive- not just replacement**.

- We do not support any ideology

- We encourage illuminated, rational, scientific, evidence-based thinking

- To push science forward for the benefit of knowledge, humans, animals and the environment

CURRENT MEMBERS

UNIVERSITÀ
DI PISA

UNIVERSITÀ
DI GENOVA

POLITECNICO
DI TORINO

CAMPUS BIOMEDICO

POLITECNICO
DI MILANO

UNIVERSITÀ
DI PAVIA

UNIVERSITÀ
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BICOCCA

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DELLE
MARCHE

UNIVERSITÀ
DI VERONA

INRIM

UNIVERSITÀ
PIEMONTE
ORIENTALE

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SCIENZE BIOMEDICHE II

Fisioterapia

Modulo	Docente
Fisiologia	Antonio Cutruzzolà

Sample size matters

Valutazione

Titolo del progetto:

Gender Matters to The Heart And Arteries: Relationship between Gender-Related Factors and Microvascular Dysfunction in Type 2 Diabetes

Codice del progetto: **P20227JBRJ**

Settore ERC: **LS7**

Principal Investigator: **Antonio CUTRUZZOLÃ€**

Ente di afferenza: **Università degli Studi "Magna Graecia" di CATANZARO**

1. Quality of the research project - scientific merit and innovative nature of the project from an international perspective - in particular:

CRITERIA	EVALUATION
a) Relevance of the project to the strategic theme and related cluster chosen by the PI (see Annex 1)	*(provide a score from 1 to 10)* **9**
b) Clarity and originality of the project's objectives	*(provide a score from 1 to 10)* **8**
c) Relevance of the proposed project to the state of art in its specific scientific area	*(provide a score from 1 to 10)* **9**
d) Consistency of the proposed methodology with the project structure and its objectives and with the specific contributions of the local units (if any)	*(provide a score from 1 to 10)* **8**

The proposal is from a team of young investigators in the south of Italy. Their publication record is heterogeneous with Dr Izzo being the one with excellent outputs. The environment is very supportive and methodologies are sound and available. To what extent is the project feasible and coherent in terms of competence, composition, and complementarity of the research team with specific regard to gender balance? The team is well sorted with attention to gender issues. The main problem is the lack of clarity in the group size in aim 1 and lack of jusification for group size in aim 2. The budget and allocation of time is fine.

Aim 1

stress and mitochondrial dysfunction, will be included as confounders or covariates. For the Project 1, we have calculated the sample size according to the coefficient of correlation available in the literature between endothelial function and traditional cardiovascular risk factors, which ranges from 0.35-0.45. Assuming a correlation coefficient between gender-related score and the measures of endothelial function of 0.40, the number of patients to achieve a power = 80% and a level of significance = 0.05 is = 36 in each group (women and male).

Aim 2

?

Reviewing…

Factors affecting the hypoglycemic confidence of individuals with type 2 diabetes using insulin: A cross-sectional study
--Manuscript Draft--

Sample size

Materials and methods

The research is a cross-sectional study. In this study, the sample size calculation formula $(n=t^2pq/d^2)$ was used in groups whose population size was uncertain. 175 individuals with type

Oscar Lodari · 1°

PhD Student presso Università "Magna
Graecia" di Catanzaro, Dietista, Dottore
Magistrale in Scienze dell'Alimentazione

TALKING WITH COLLEAGUES...

Question

"**How many** patients do we need?»

Answer

"**Never enough**!»

WHY DO WE NEED SAMPLE SIZE CALCULATIONS?

Important **practical** reasons…

Possibility of detecting effects

Preventing resources waste

Ethics

WHY WE DO NEED SAMPLE SIZE CALCULATIONS?

Too small sample size

- We **cannot demonstrate** the **effect** we want

- **Unethical** - do not treat patients optimally

Too large sample size

- **Resource wasting**

- **Unethical** – do not treat patients optimally

A PRACTICAL EXAMPLE...

Original Investigation | Nutrition, Obesity, and Exercise

An Energy-Reduced Mediterranean Diet, Physical Activity, and Body Composition
An Interim Subgroup Analysis of the PREDIMED-Plus Randomized Clinical Trial

Jadwiga Konieczna, PhD; Miguel Ruiz-Canela, PhD; Aina M. Galmes-Panades, PhD; Itziar Abete, PhD; Nancy Babio, PhD; Miquel Fiol, MD, PhD; Vicente Martín-Sánchez, MD, PhD; Ramón Estruch, MD, PhD; Josep Vidal, MD, PhD; Pilar Buil-Cosiales, MD, PhD; Jesús F. García-Gavilán, PhD; Manuel Moñino, BSc; Alba Marcos-Delgado, PhD; Rosa Casas, PhD; Romina Olbeyra, PhD; Montserrat Fitó, MD, PhD; Frank B. Hu, MD, PhD; Miguel Ángel Martínez-Gonzalez, MD, PhD; J. Alfredo Martínez, MD, PhD; Dora Romaguera, PhD; Jordi Salas-Salvadó, MD, PhD

1521 participants, mean age 65yo.

A PRACTICAL EXAMPLE...

Table 2. Effect of the PREDIMED-Plus Intervention on Body Composition Changes Over Follow-Up Time in Participants

| | Model 1 (adjusted) | | Between-group-difference | |
| | Mean change (95% CI) | | | |
Variable	Changes in intervention (n = 760)	Changes in control (n = 761)	Mean difference in changes (95% CI)	P value[b]
Primary outcomes				
Total fat mass, %				
Year 1 vs baseline	−1.14 (−1.33 to −0.96)	−0.21 (−0.39 to −0.03)	−0.93 (−1.19 to −0.68)	<.001
Year 3 vs baseline	−0.52 (−0.71 to −0.33)	−0.14 (−0.33 to 0.04)	−0.38 (−0.64 to −0.12)	
Total lean mass, %				
Year 1 vs baseline	1.08 (0.90 to 1.25)	0.20 (0.03 to 0.38)	0.87 (0.63 to 1.12)	<.001
Year 3 vs baseline	0.47 (0.29 to 0.66)	0.13 (−0.04 to 0.31)	0.34 (0.09 to 0.59)	
Visceral fat mass, g				
Year 1 vs baseline	−150 (−188 to −112)	−26.9 (−64.1 to 10.4)	−123 (−177 to −70.2)	<.001
Year 3 vs baseline	−72.2 (−112 to −32.3)	−5.50 (−43.9 to 32.9)	−66.7 (−122 to −11.3)	