

# From Project to Paper: *Meet the Editors of Cardiovascular Research*

**Study Design: It all starts here!**

*He/she who is without sin can cast the first stone....*

Disclosures:

[www.explorable.com](http://www.explorable.com)

[www.wikipedia.com](http://www.wikipedia.com)

# Scope of Cardiovascular Research

- Cardiovascular Research is the international journal of the ESC for basic and translational research, across different disciplines and areas
- ....papers at the molecular, sub-cellular, cellular, organ, and organism level, and clinical proof-of-concept and translational studies
- ....to enhance insight in cardiovascular disease mechanisms and the perspective for innovation
- ....provide a significant contribution to the field with relevance for cardiovascular biology and diseases

# Study Design

- The design is the structure of any scientific work; it gives direction and systematizes the research
- Research design is the framework that is created to seek answers to research questions
- There is a variety of designs:
  - Descriptive Designs (e.g. case study)
  - Correlational Studies
  - Semi-Experimental Designs
  - *Experimental*
  - Reviewing (Systematic Reviews)
  - Meta-Analysis

# Experiment

- An experiment is a procedure carried out to verify, refute, or validate a *hypothesis*
- Experiments *provide insight into cause-and-effect* by demonstrating what outcome occurs when a particular factor is manipulated
- Experiments vary greatly in goal and scale, but always rely on *repeatable procedure* and *logical analysis* of the results.



# Experimental Design

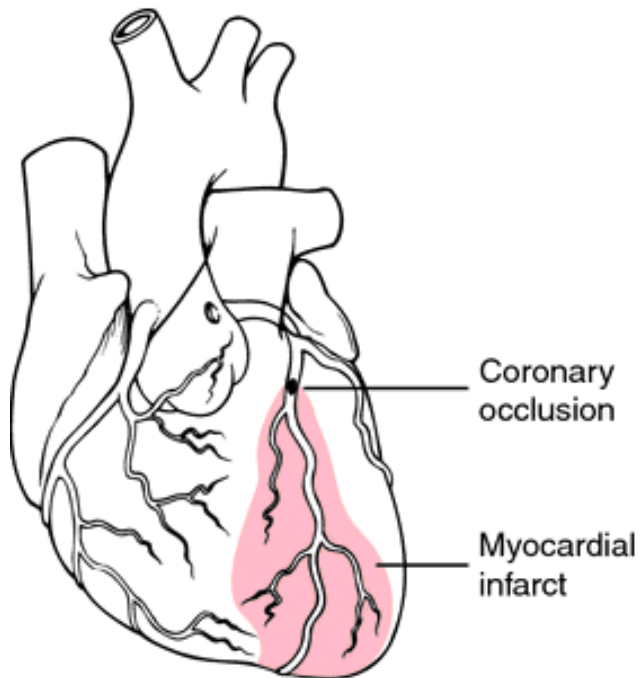
- How many *factors* does the design have?
- Are these factors *fixed or variable*?
- What is the relevance of *interactions* between factors?
- Are *control* conditions needed, and what should they be?
- Test efficacy of *interventional tools*
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# Factorial design

- Factor 1 = Ischemic preconditioning stimulus (PC)
- Factor 2 = Adenosine receptor blockade (SPT)



Control

SPT

Sham

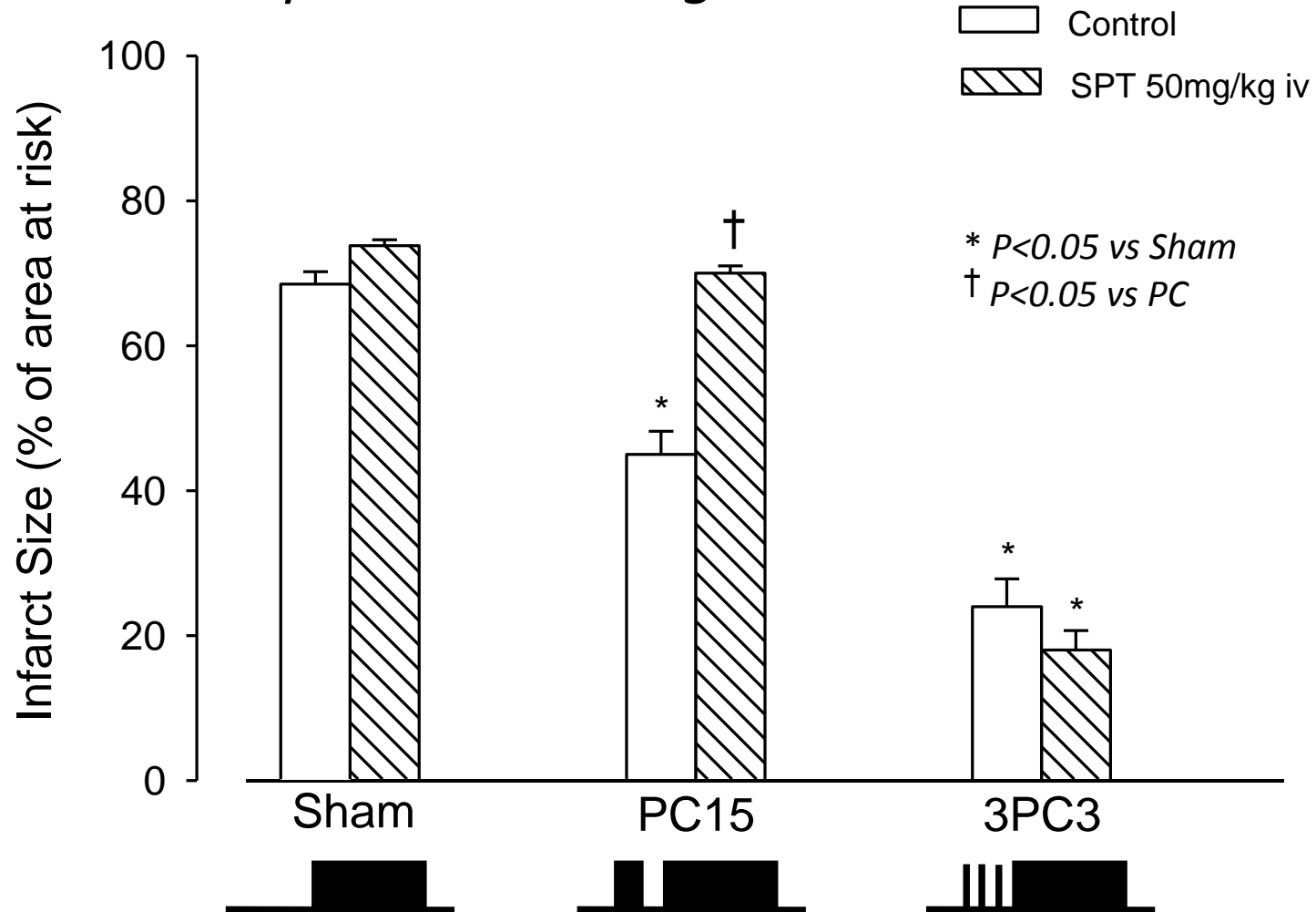
PC15

3PC3




# Factorial Design

## *Adenosine in preconditioning*





# Factorial design

## 2 x 7 design

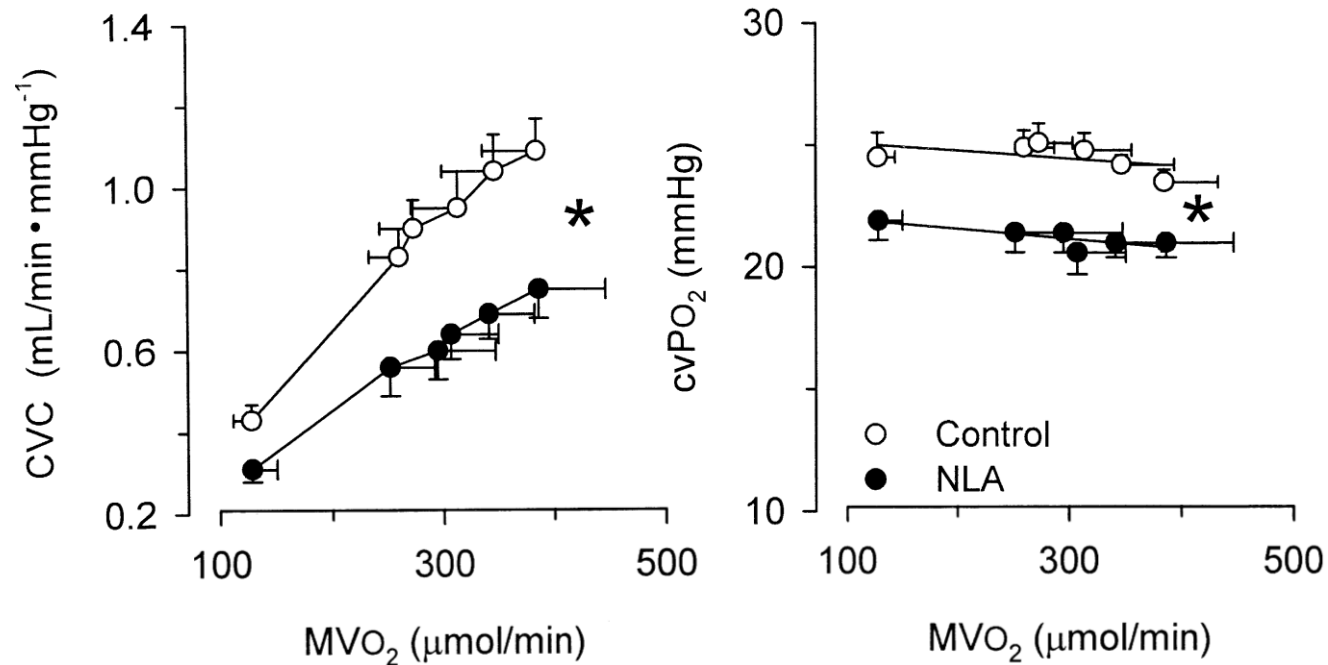
- Factor 1 = NO synthase inhibition (Control and NLA)
- Factor 2 = Physical activity (7 levels of physical activity)

Hemodynamic effects of NO synthase inhibition<sup>a</sup>

		Rest		Exercise (km/h)				
		Lying	Standing	1	2	3	4	5
<i>Systemic</i>								
HR (bpm)	Control	116±6	135±6*	165±7*	184±8*	200±6*	231±6*	254±5*
	NLA	93±5†	119±5*†	135±4*†	146±5*†	164±7*†	190±8*†	218±5*†
MAP (mmHg)	Control	101±2	90±2	92±1	89±1	92±1	91±2	92±2
	NLA	132±4†	122±2†	125±2†	127±3†	126±2†	124±2†	122±2†
CO (l/min)	Control	3.7±0.2	5.0±0.3*	6.0±0.3*	6.5±0.3*	7.0±0.3*	7.5±0.3*	8.1±0.3*
	NLA	2.8±0.2†	4.1±0.3*†	4.9±0.3*†	5.2±0.3*†	5.8±0.4*†	6.6±0.3*†	7.4±0.4*†
SVC (ml/min mmHg <sup>-1</sup> )	Control	37±2	56±4*	65±3*	73±4	76±4*	82±3*	88±3*
	NLA	22±1†	34±3*†	40±3*†	41±3*†	46±3*†	53±3*†	60±3*†
LVdP/dt <sub>max</sub> (mmHg/s)	Control	3030±180	3450±210*	4250±300*	4520±280*	5010±320*	5630±240*	6090±240*
	NLA	2330±110†	2970±150*†	3490±180*†	3870±220*†	4610±280*	5720±410*	6690±330*†
LVSP (mmHg)	Control	119±4	118±3	124±3*	126±2*	131±3*	135±3*	142±4*
	NLA	149±5†	145±5*†	147±3*†	149±4*†	151±3*†	155±4*†	159±3*†

# Factorial design

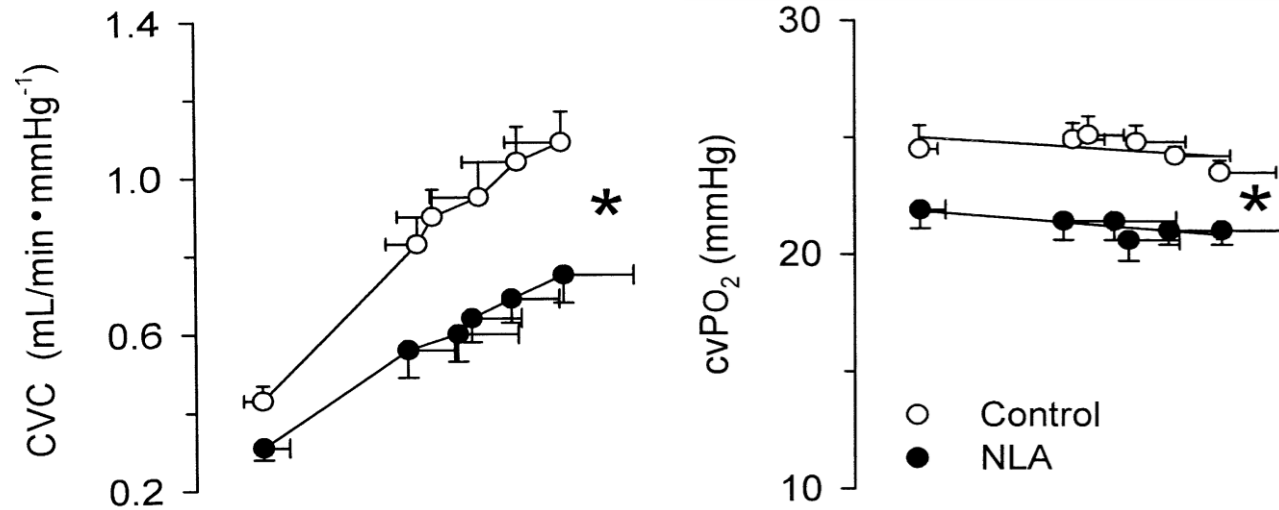
- Variable factors



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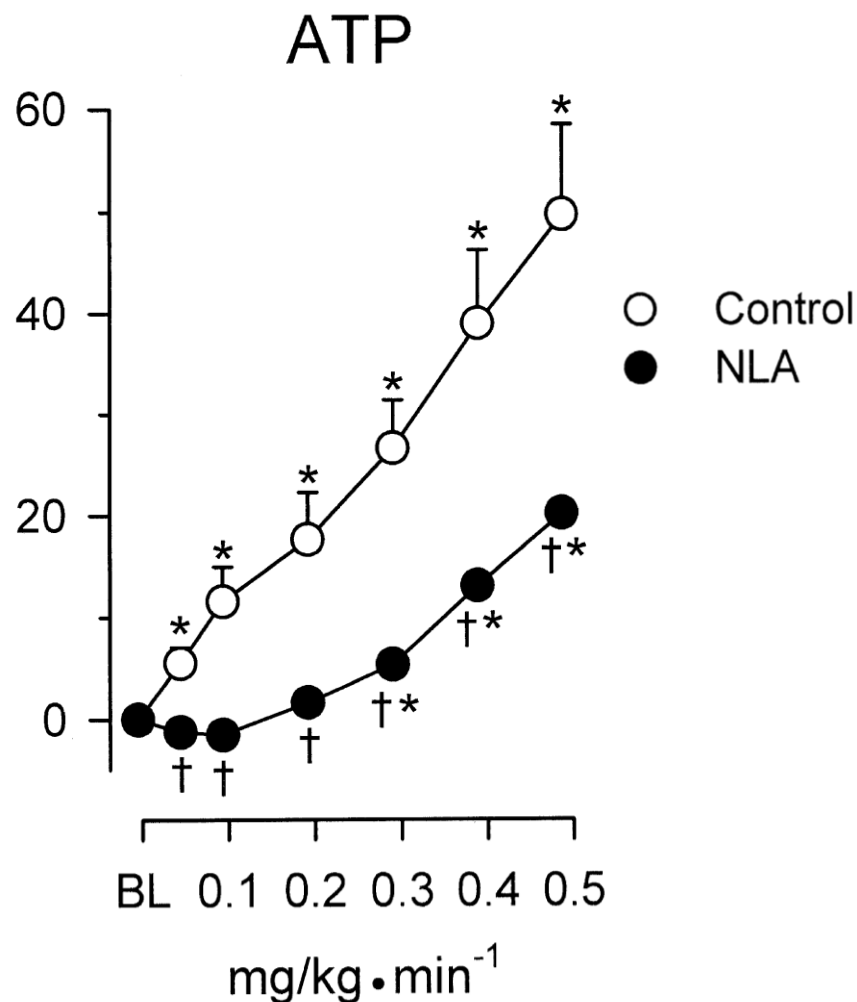
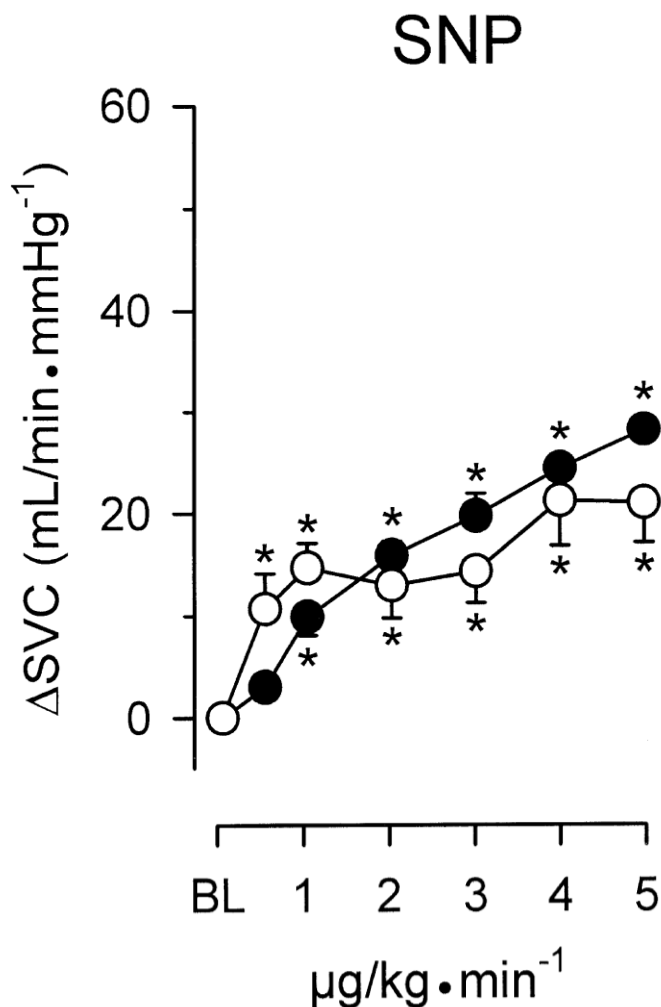
# Importance of control conditions



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# Test efficacy of interventional tools

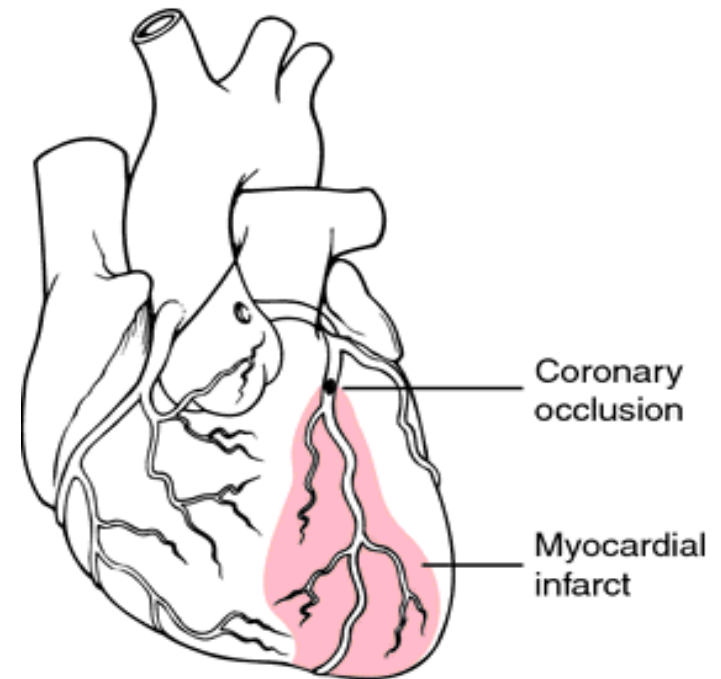


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# Taking background factors into account

- Ischemia time
- Area at Risk
- Collateral flow
- Temperature
- Hemodynamics
- Timing of treatment



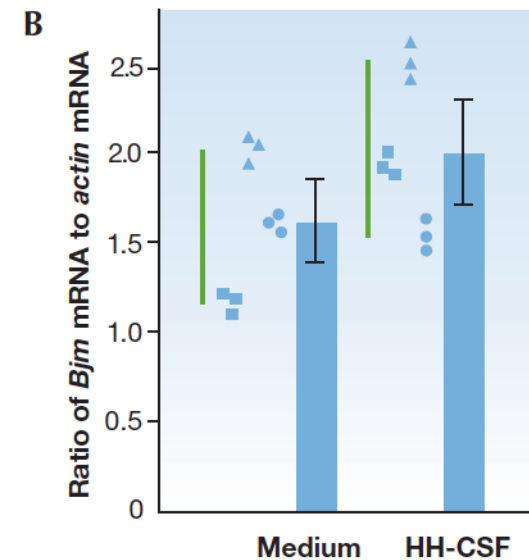
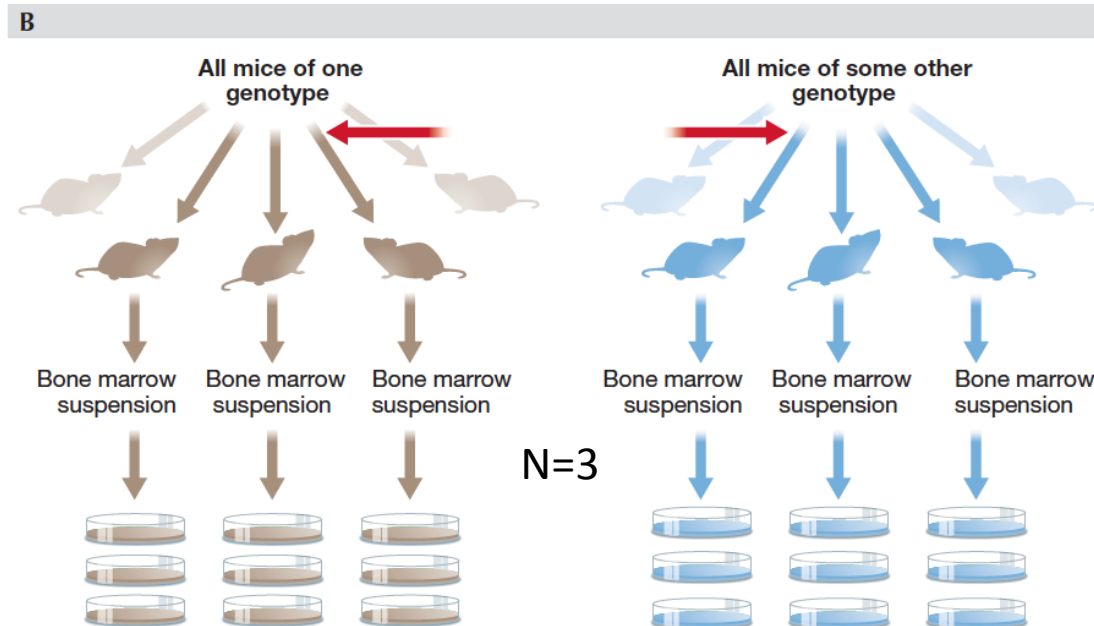
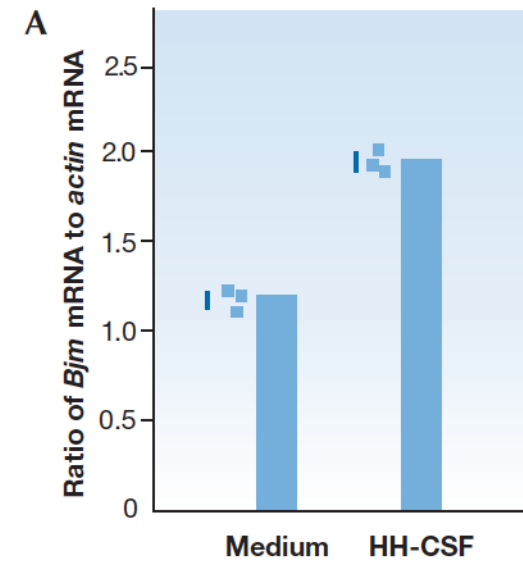
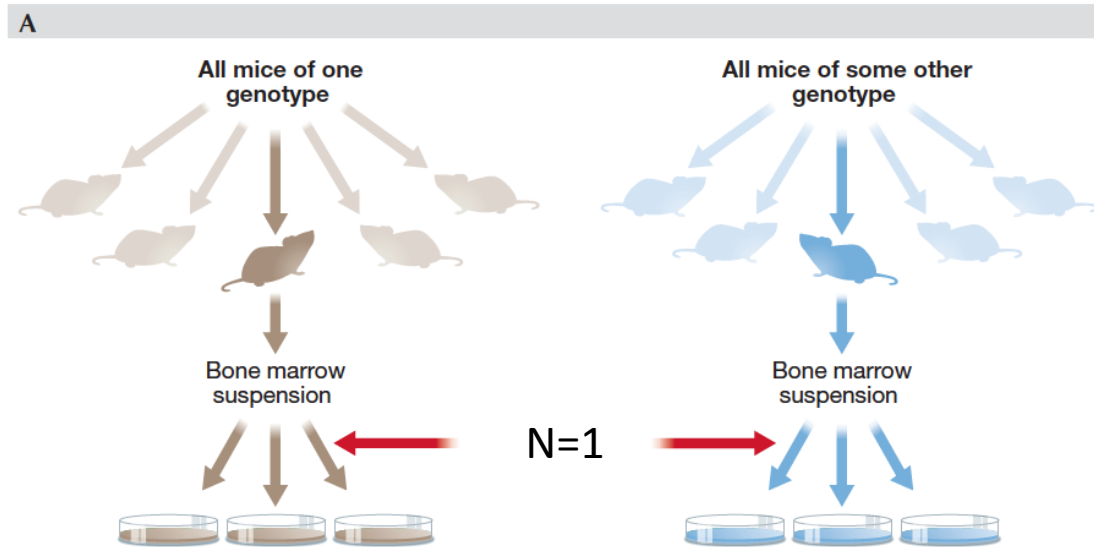


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# Technical Replicates versus Biological Repeats

Vaux et al., *EMBO Reports* 2012;13:291-296



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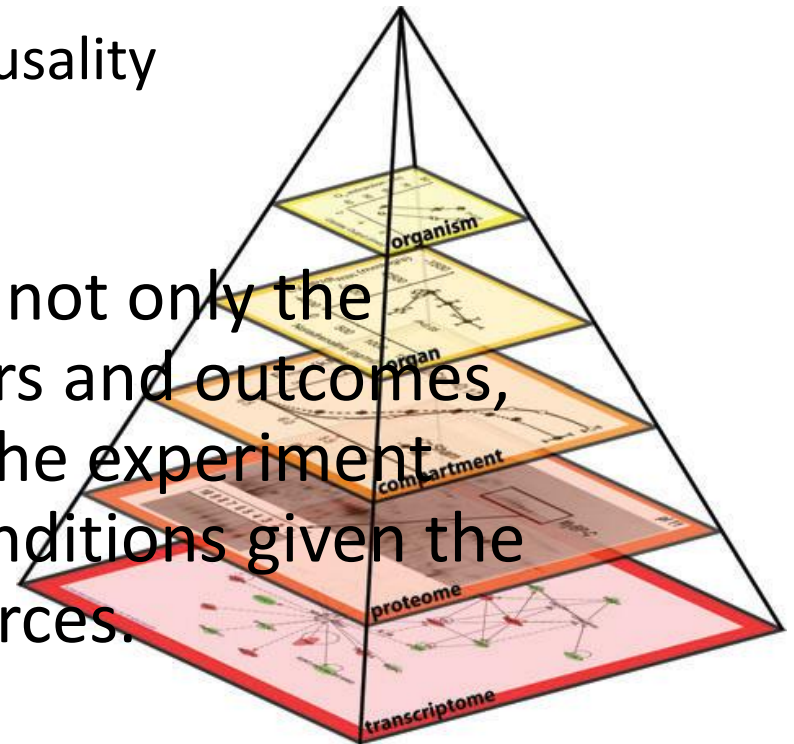
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# Study Design: Enhancing Impact

## ➤ Multilayered studies

- Multiple species (human)
- Multiple platforms: in silico, in vitro and in vivo
- Multiple technologies
- Multiple lines of evidence of causality
- Healthy and diseased states

## ➤ Experimental design involves not only the selection of suitable predictors and outcomes, but planning the delivery of the experiment under statistically optimal conditions given the constraints of available resources.



# Conclusions

Proper design is extremely important:

- Control conditions
- Interventional tools
- Background variables
- Sample size
- Technical replicates vs biological repeats
- Multilevel approach to enhance impact

➤ *Within the constraints of available resources*