Impact of nanocelluloses on genome-wide DNA methylation pattern of human pulmonary and intestinal cells

6th CHRC Annual Summit

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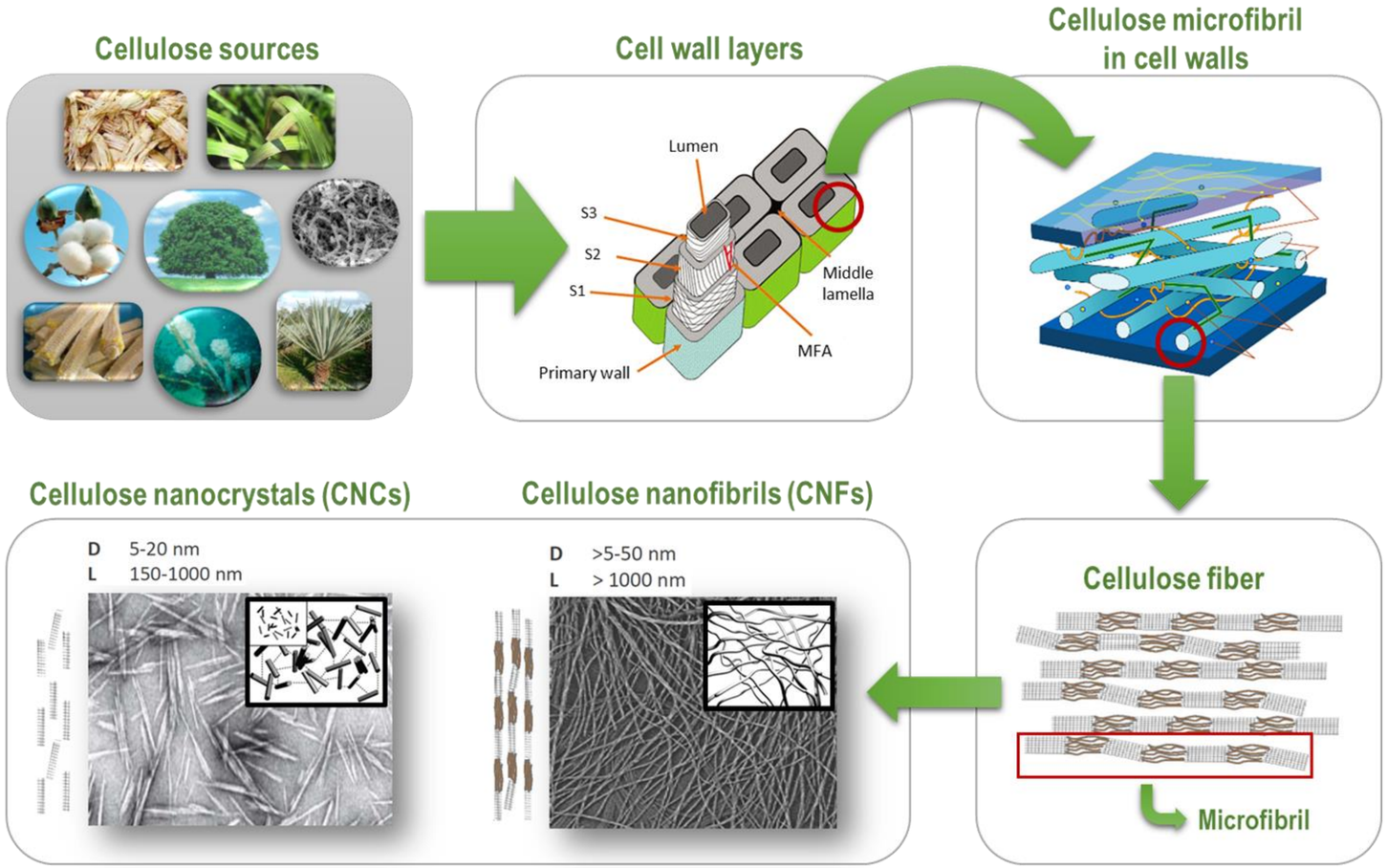
Nanocellulose

Nanomaterial

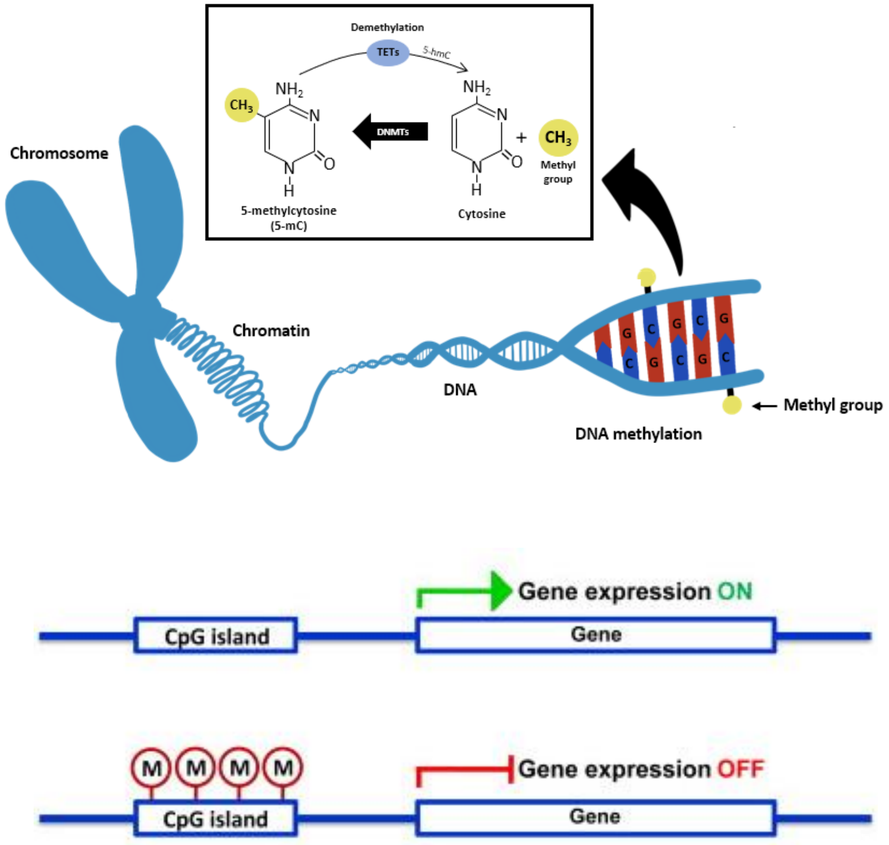
A natural or manufactured material, composed of solid particles that are present alone, in aggregates or agglomerates, and where at least 50% of these particles have **dimensions between 1 and 100 nm**.
(European Commission, 2022)



- Potential use for a wide variety of industrial (packaging, paper industry and others) and biomedical applications (regenerative medicine, wound healing, drug delivery systems and others).

- Toxicity studies, mainly *in vitro*, revealed biocompatibility, but others genotoxic or inflammatory effects. No epigenomics studies.

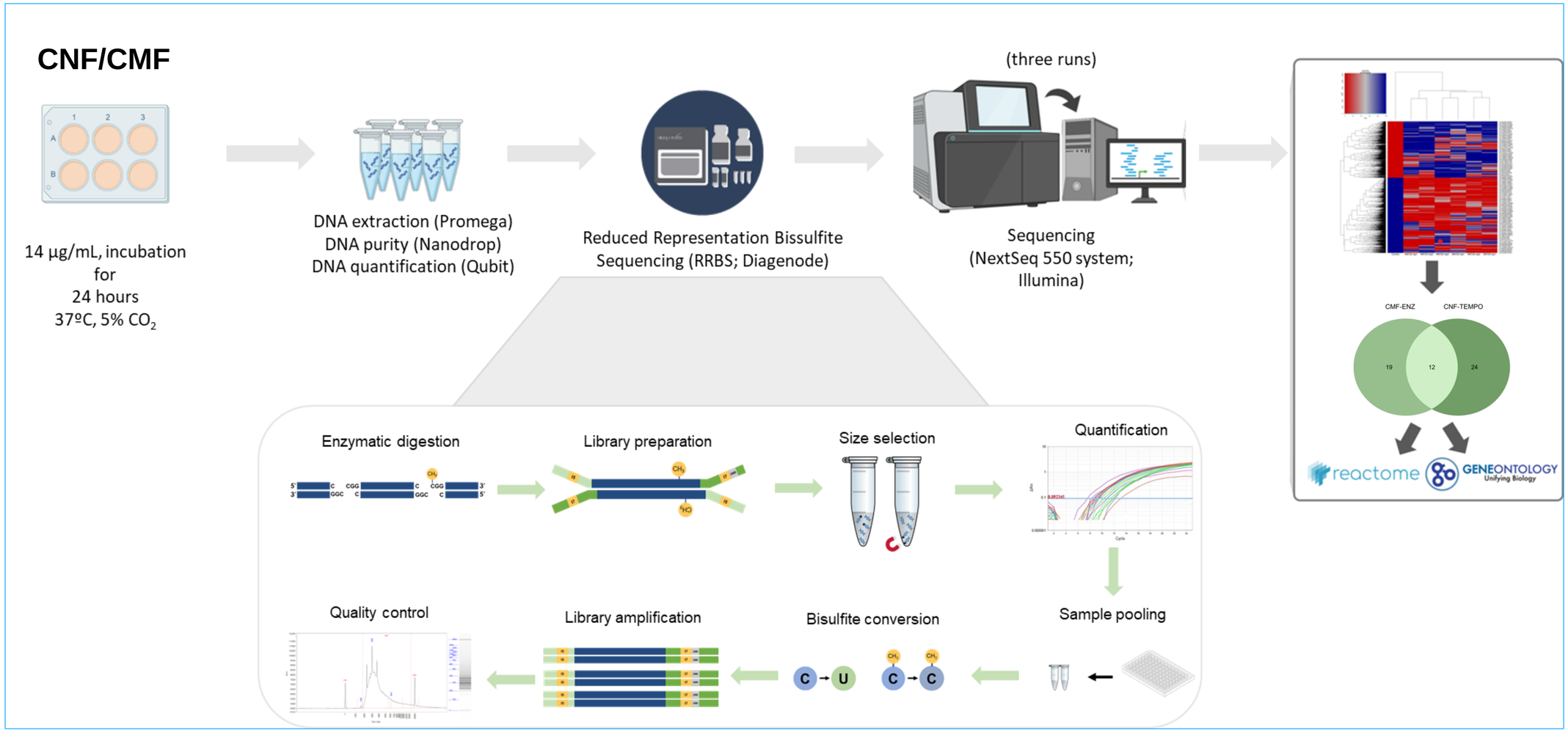
DNA methylation and gene expression regulation



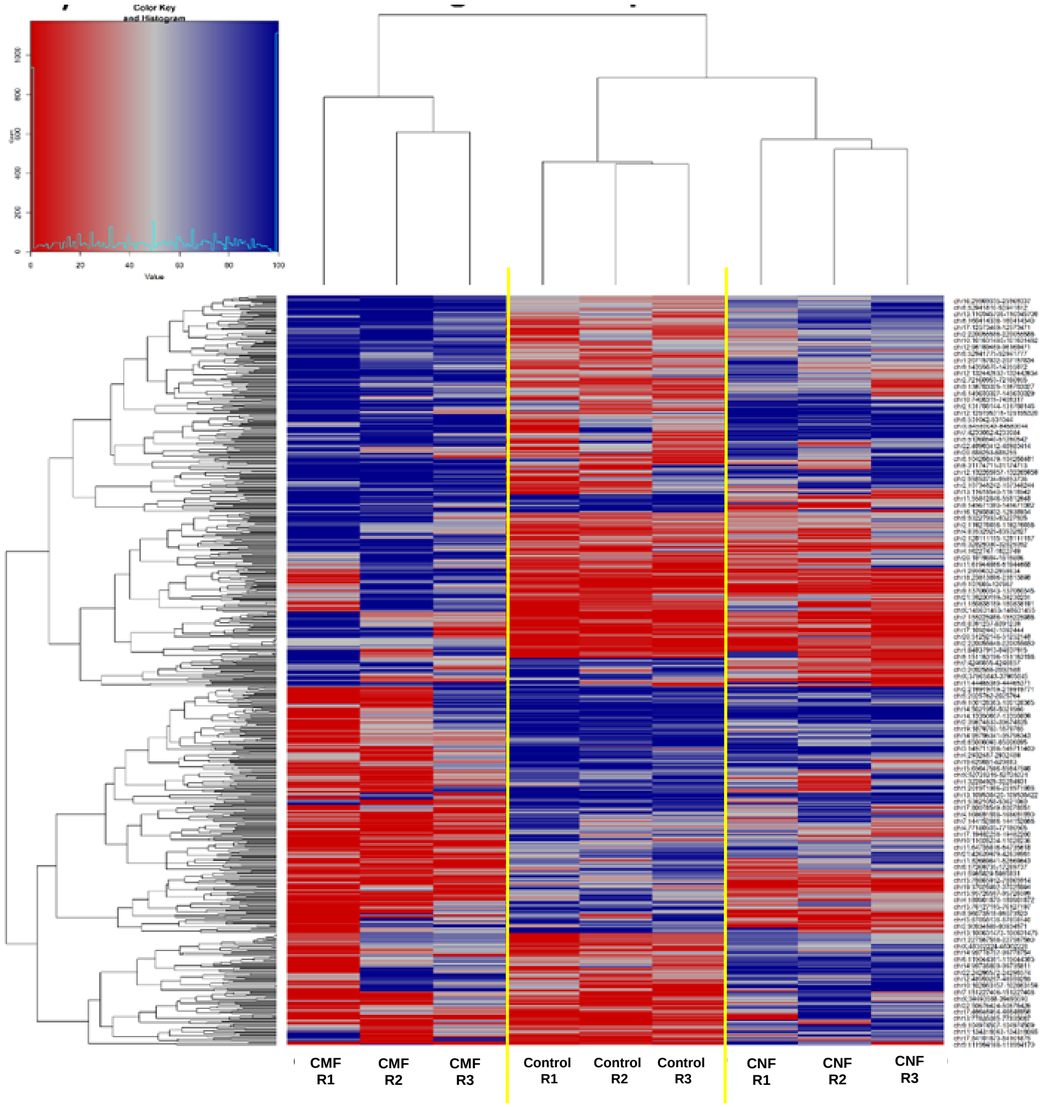
Adapted from Pal et al, microRNA in Regenerative Medicine, Academic Press, 2015, 77-109,

- ✓ Addition of methyl groups to the cytosine of CpG dinucleotides
- ✓ In mammalian somatic cells, 70-80% of CpG sites are methylated, but CpG islands, which are usually near gene promoter regions, are often unmethylated to allow for gene expression.
- ✓ Gene promoter methylation can result in down-regulation of gene expression by blocking transcription initiation.

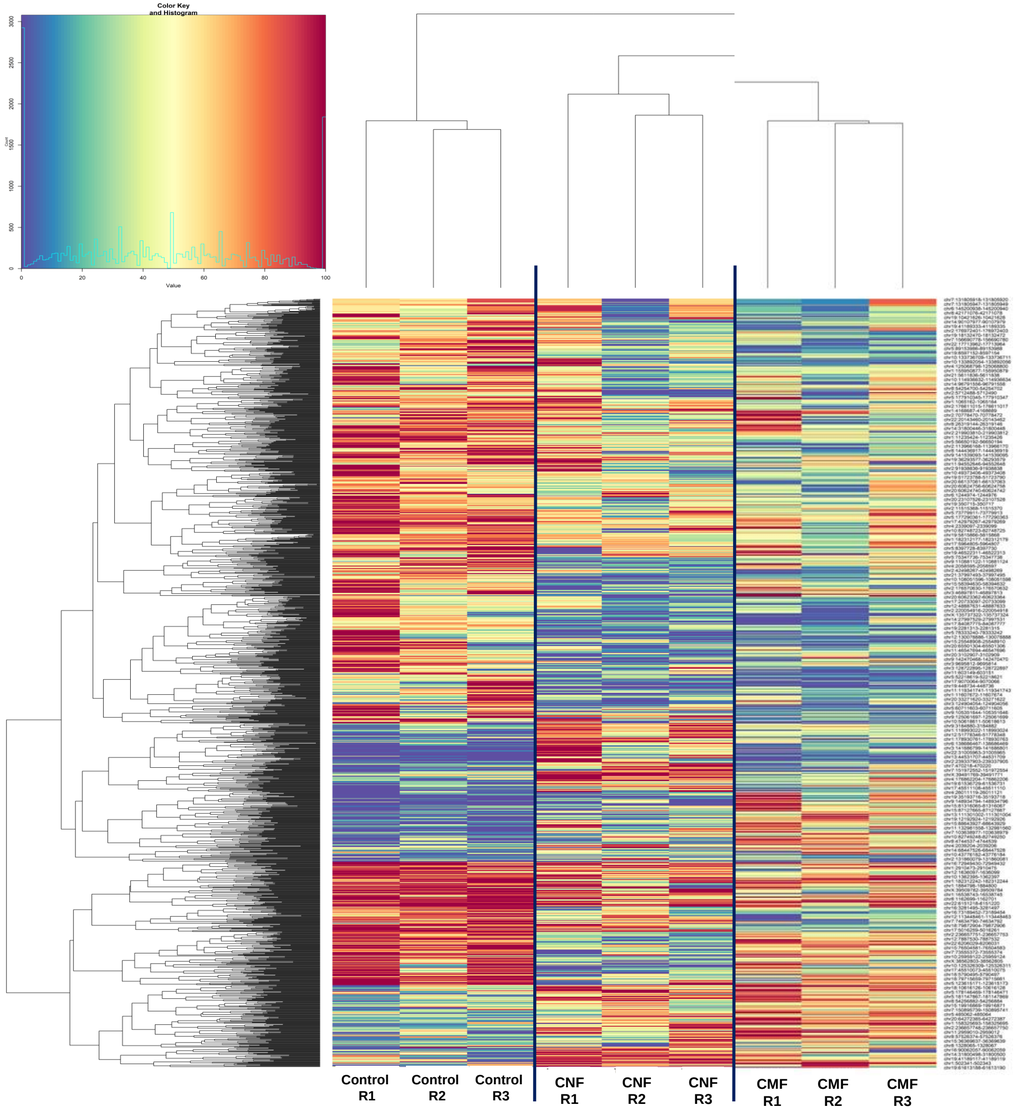
Methodology



Results



Caco-2 cells



BEAS-2B cells

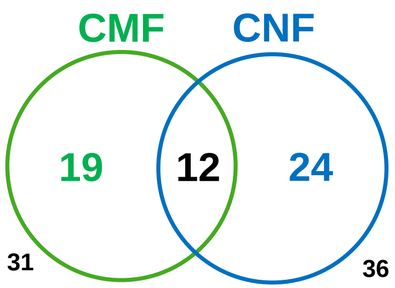
Results

	Caco-2		BEAS-2B	
	CMF	CNF	CMF	CNF
Hypomethylated	3	4	17	11
Hypermethylated	56	80	2	1
Total	**59**	**84**	**19**	**12**

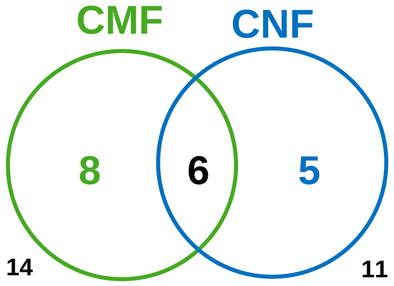
Differentially methylated genes

Common genes
ARHGAP45
CABIN1
FAM217B
GPC1
GPC1-AS1
KDM2B
LRFN1
NAPRT
NID1
OBSL1
ZBTB45
POLR1C

Caco-2



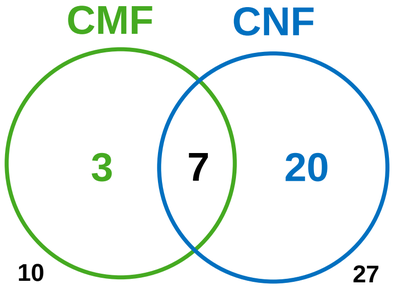
BEAS-2B



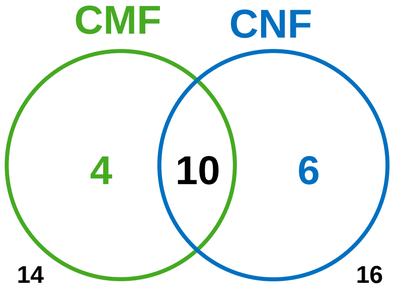
Common genes
ARHGAP22
DYRK1B
TERT
TNXB
PLAGL1
GRB10

reactome

Caco-2

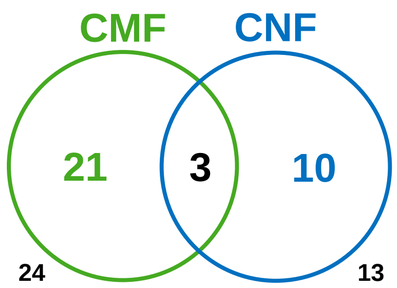


BEAS-2B

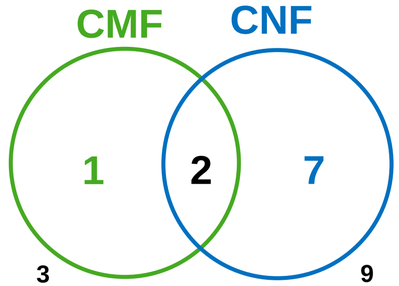


GENEONTOLOGY
Unifying Biology

Caco-2



BEAS-2B



In summary…

Intestinal Caco-2 cells

CMF

- DNA repair
- **Glycosaminoglycan metabolismo/O-glycosylation**
- **Cell proliferation, motility and migration** (cytoskeletal and extracelular matrix dynamics)
- Gene expression regulation (binding to transcription regulatory regions)

CNF

- **Glycosaminoglycan metabolismo/O-glycosylation**
- Regulation of metabolism glucagon / insulin regulation
- **Cell proliferation, motility and migration**
- Ligand binding to cell surface and laminin
- Cellular responses to stimuli (e.g., metal ions)

Pulmonary BEAS-2B cells

CMF

- **Regulation DNA replication, damage repair and senescence**
- **TP53 cell cycle regulation**
- **Telomere extension**
- **Insulin signalling**
- Potassium chanells
- **Regulation of D-glucose transport**

CNF

- **Regulation DNA replication, damage repair and senescence**
- **TP53 cell cycle regulation**
- **Telomere extension**
- **Insulin signalling**
- Tyrosine kinase receptor activity
- **Regulation of D-glucose transport**

✓ Nanocellulose has a different molecular effect on diferent cell types

✓ CMF and CNF have a different molecular effect on the same cell type, which may be a consequence on their physical-chemical characteristics

✓ DNA methylation is a powerful approach to explore the adverse effects of nanomaterials, opening many doors to further research.

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