



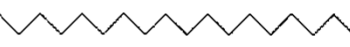
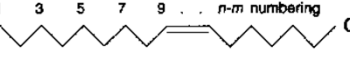
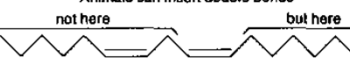
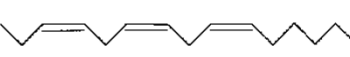
➤ PUFA as tool to improve fertility: hype or significant benefit?

Sébastien ELIS

UMR Physiology of Reproduction and Behaviors,
Centre INRAE Val de Loire, France

Fatty acids

Number and position of double bonds

		Methyl	Carboxyl	
Saturated fatty acids	SFA	CH ₃		COOH
Monounsaturated fatty acids	MUFA	CH ₃		COOH
Polyunsaturated fatty acids	n-6 PUFA	CH ₃		COOH
	n-3 PUFA	CH ₃		COOH

Annotations for PUFA chains:

- For Oleic Acid: Carbons 1, 3, 5, 7, 9 are numbered. The double bond is at C9, labeled "n-m numbering".
- For Linoleic Acid: Brackets indicate "not here" between C6 and C9, and "but here" between C9 and C12. Text above says "Animals can insert double bonds".

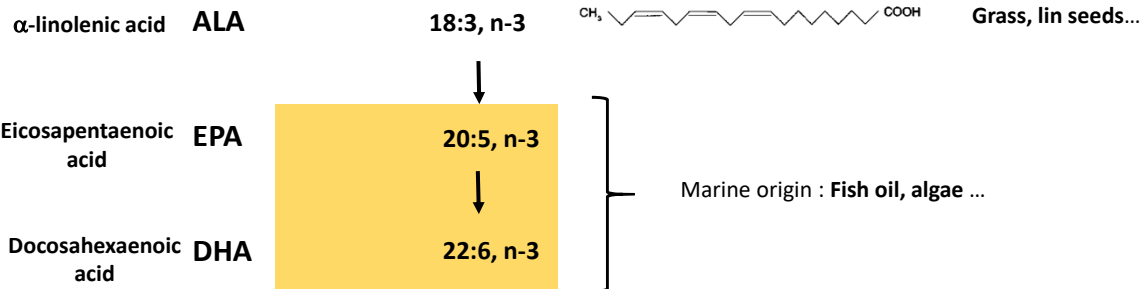
Essential fatty acids (indicated by a bracket on the right): n-6 PUFA and n-3 PUFA.

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n-3 PUFA



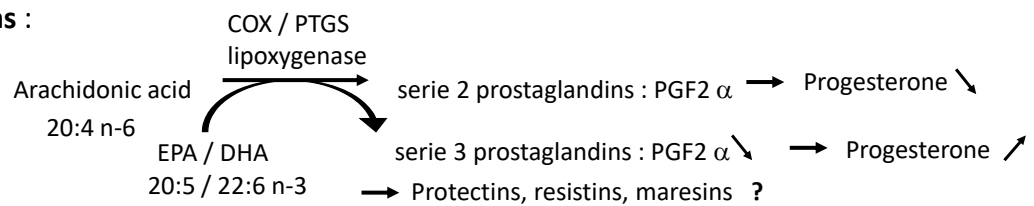
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How does it work?

Prostaglandins :



Membrane structure/composition: elasticity

Signal transduction: lipid rafts

Activation of **specific receptors:** fatty acid receptors

Calder 2012, J Nutr, 142:592S-599S

Calder 2015, Biochim and Biophys Acta, 1851:469-484

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n-3 PUFA supplementation and reproduction

In vitro (oocyte maturation medium)

Increased embryo developmental rates

In vivo experiments :

Greater pregnancy rate

Lower early embryo mortality

Decrease in PGF2 α (uterus level)

→ facilitating embryo implantation

Increase in pre-ovulatory follicle size

in small follicle number

improve embryo production

2 reviews :

Dietary fat Leroy et al. 2014, RDA, 49:353-361

N-3 PUFA Moallem 2018, JDS, 101:8641-8661

Marei et al. 2009, Biol Reprod, 81:1064-1072

Petit and Twagiramungu 2006, Therio, 66:1316-1324

Dirandeh et al. 2013, JAS, 91:713-721

Sinedino et al. 2017, Reproduction, 153:707-723

Mattos et al. 2004, JDS; 87:921-932

Ambrose et al. 2006, JDS, 89:3066-3074

Zachut et al. 2010, JDS, 93:529-545

Moallem et al. 2013, Reproduction, 146:603-614

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n-3 PUFA supplementation

Discrepancies / confounders

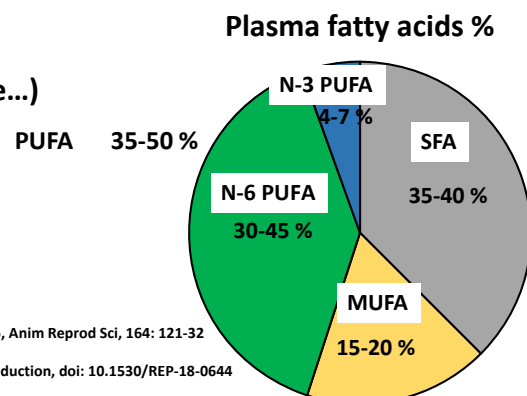
- negative effects on reproduction
- FA, dose, form (ruminal protection?), duration, physiological stage ...

Hutchinson et al. 2012, Therio, 78:12-27

- control used in the study
- SFA (palmitic acid)
- n-6 PUFA (linoleic acid: soy, maize...)



also positive effects



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Objectives:

- Investigate EPA / DHA effects on oocyte quality
- AI, embryo production, *in vitro* studies
- Comparison with n-6 PUFA
- Moderate dose, several diet duration (folliculogenesis stage)

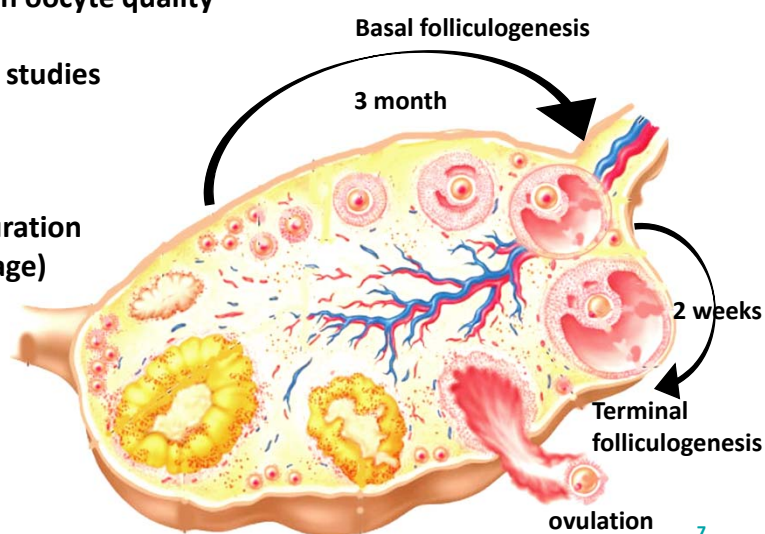
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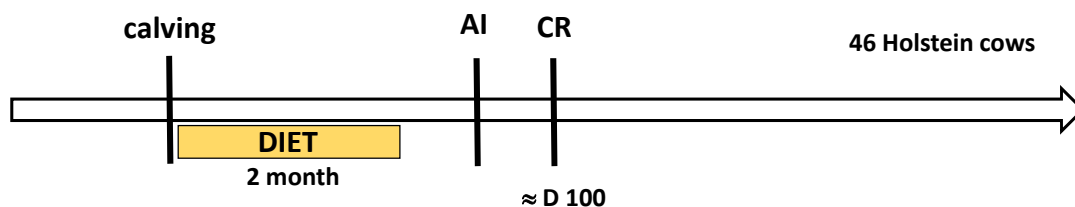
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Experimental designs:**Effects on fertility through the oocyte?**

Exp 1



- 3 month for an oocyte to grow and mature (basal folliculogenesis targeted)
- The diet could affect oocyte growth BUT not embryo implantation (high n-3 PUFA clearance during lactation)

→ Follicular population and conception rates after the 1st AI

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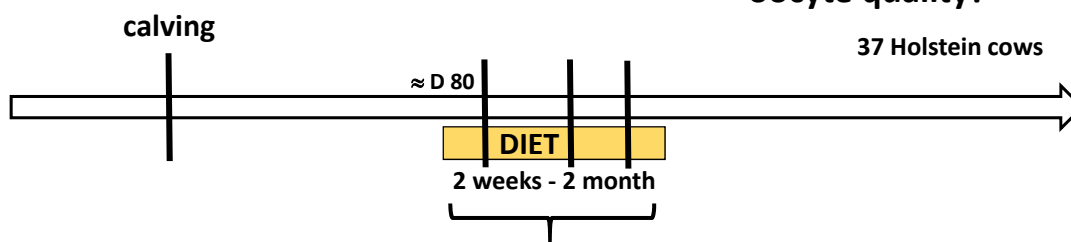
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Elis et al. 2016, Anim Reprod Sci, 164: 121-32

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Experimental designs:**Effects on embryo production ?
oocyte quality?**

Exp 2



OPU sessions : oocyte collection → embryo production

- Both basal and terminal folliculogenesis targeted
- Several durations

→ Developmental rates

Rumen protected Fish oil 1% DMI EPA + DHA
Rumen protected Soy oil 1% DMI n-6 PUFA

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Freret et al. 2019, Reproduction, doi: 10.1530/REP-18-0644

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Experimental designs:

In vitro exp.

Effects on oocyte quality?

DHA supplementation in IVM medium during 24h



Developmental rates

- Terminal folliculogenesis only
- Several concentrations
- Insight on mechanisms of action

Oseikria et al. 2016, Therio, 85:1625-1634

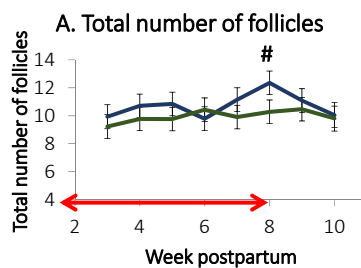
Elis et al. 2017, J Ovarian Res, 10:74

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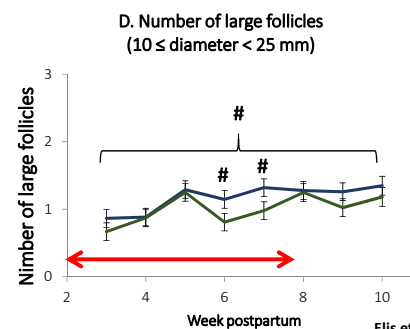
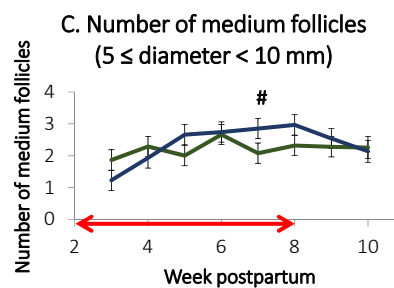
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Results:



Increase in number of follicles



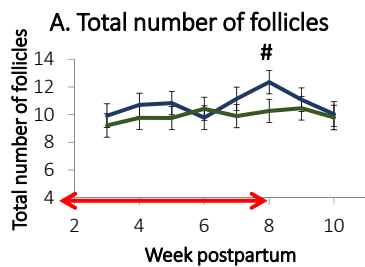
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Elis et al. 2016, Anim Reprod Sci, 164: 121-32

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Results:



Conception rates

	n-3	n-6	p-value
NF-EEM	13.5	38.8	0.086 #
CRAI1 35D after AI1	72.9	48.5	0.129
CRAI1 90D after AI1	56.1	48.1	0.629

Increase in number of follicles

Reduction in the non fertilization – early embryo mortality %

Ovarian effects (not only through uterus and prostaglandins)

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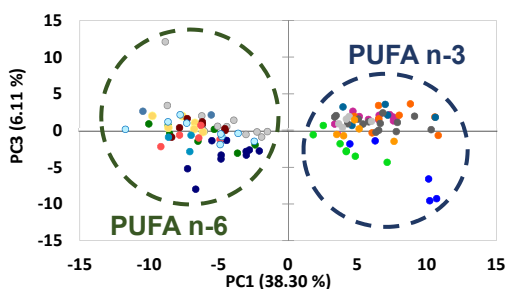
Elis et al. 2016, Anim Reprod Sci, 164: 121-32

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Results:

Embryo production

Oocyte lipid composition



	n-3	n-6	p-value
% recovered COC	38.0±1.6 *	32.8±1.6	0.0035
% cleaved embryos	77.3±3.8 #	82.3±3.3	0.1033
% blastocysts	49.6±5.5 #	42.3±5.5	0.0865
% blastocyst Q1-Q2	42.2±7.7 *	32.7±7.1	0.0217

Increase in blastocyst rate (freezable quality)

Diet : changes in oocyte lipid composition

A short duration of supplementation might be enough (less than a month)

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Freret et al. 2019, Reproduction, doi: 10.1530/REP-18-0644

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Results:***In vitro* experiment : DHA in IVM – 24h**

Control	% blastocysts			
DHA 1 μ M	17.6 \pm 3.3			
	30.6 \pm 4.1	p<0.05	→	DHA 1 μ M improves blastocyst rate No effect of DHA 10 μ M Toxic effect of DHA 100 μ M

Oseikria et al. 2016, Therio, 85:1625-1634

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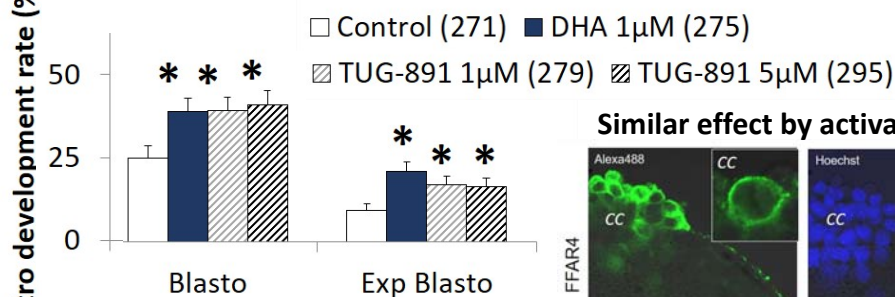
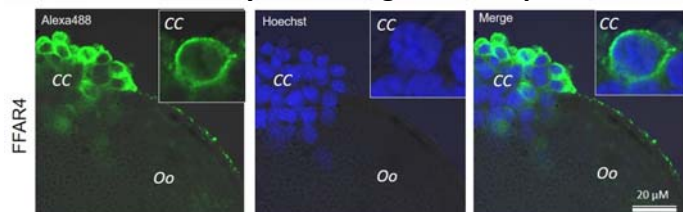
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**Similar effect by activating a FA receptor : FFAR4**

Elis et al. 2017, J Ovarian Res, 10:74

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Are n-3 PUFA supplementations effective ?

- ✓ **N-3 PUFA supplementation is effective**
 - enhancement in reproductive parameters (most of the studies)
action through ovary and not only uterus
 - even when compared to n-6 PUFA

BUT

- ✓ **Moderate improvement only**
- ✓ **High cost / competition with human feed – limited resources**
18-20€/kg → grass, lin seed, algae (similar efficiency?)

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Take-home messages :

- ✓ **N-3 PUFA → positive effects on the oocyte quality**
- ✓ **Interesting when dealing with moderate quality oocyte**
(→ high genetic merit cows)

BUT

- ✓ **Cost - benefit evaluation depends on your activity**
- ✓ **Embryo producing companies : low cost solutions, short supplementation**
- ✓ **Farms : too expensive for reproduction purpose only**
(→ increasing dairy product value : n-3 enriched products ?)

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Thank you for your attention

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Funding



Etc...

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APIS-GENE
investir. Innover. Valoriser.

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