

# The Interreg NWE Project **Codex4SMEs**:

## Webinar rules

1. Switch off your camera and your microphone.
2. During the whole webinar, only the speakers will be allowed to talk.
3. Ask questions via the CHAT.
4. **If you cannot hear the speaker please inform us via CHAT. Alternatively, use the dial-in number:**



# Interreg NWE Project Codex4SMEs Introduction

Webinar, 4<sup>th</sup> of February, 2021

**Pablo Zardoya-Laguardia, PhD**

Biobank Graz (Medical University)

# Interreg North-West Europe

EUROPEAN UNION

## Interreg NEW Programme

European Territorial Cooperation programme with the ambition to make the North-West Europe area a key economic player and an attractive place to work and live, with high levels of innovation, sustainability and cohesion.

# Codex4SMEs Project

## Codex4SMEs

= **Companion diagnostics expedited for (4) Small and Medium Enterprises**

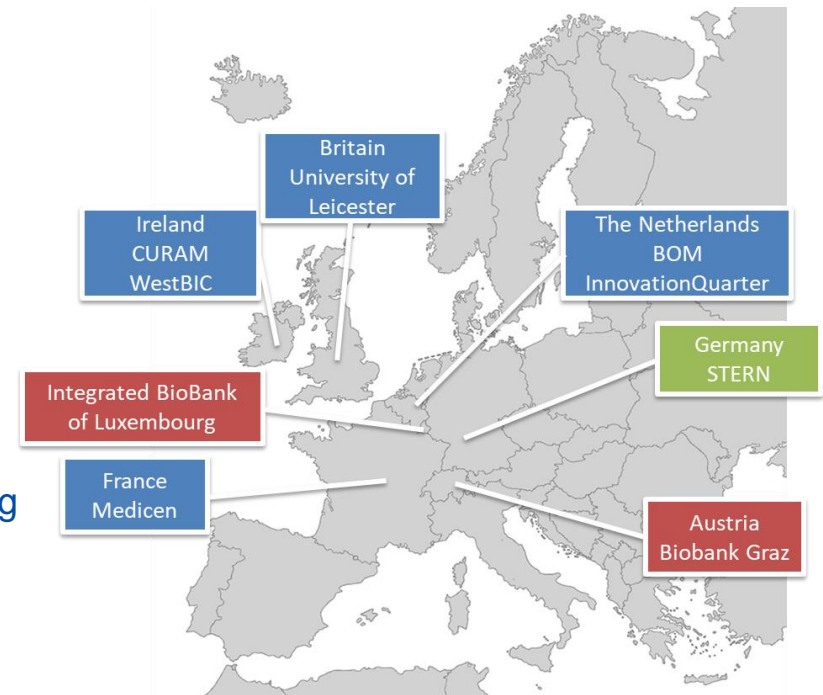
**Total budget:** 3 M €  
**ERDF budget:** 2 M €  
**Project period:** 36 months

### Objective of the project:

- Improve healthcare by enhanced adoption of Personalized Medicine
- Establishing a network which supports SMEs along the value chain of Companion diagnostics (Cdx) development

### Associated Partner:

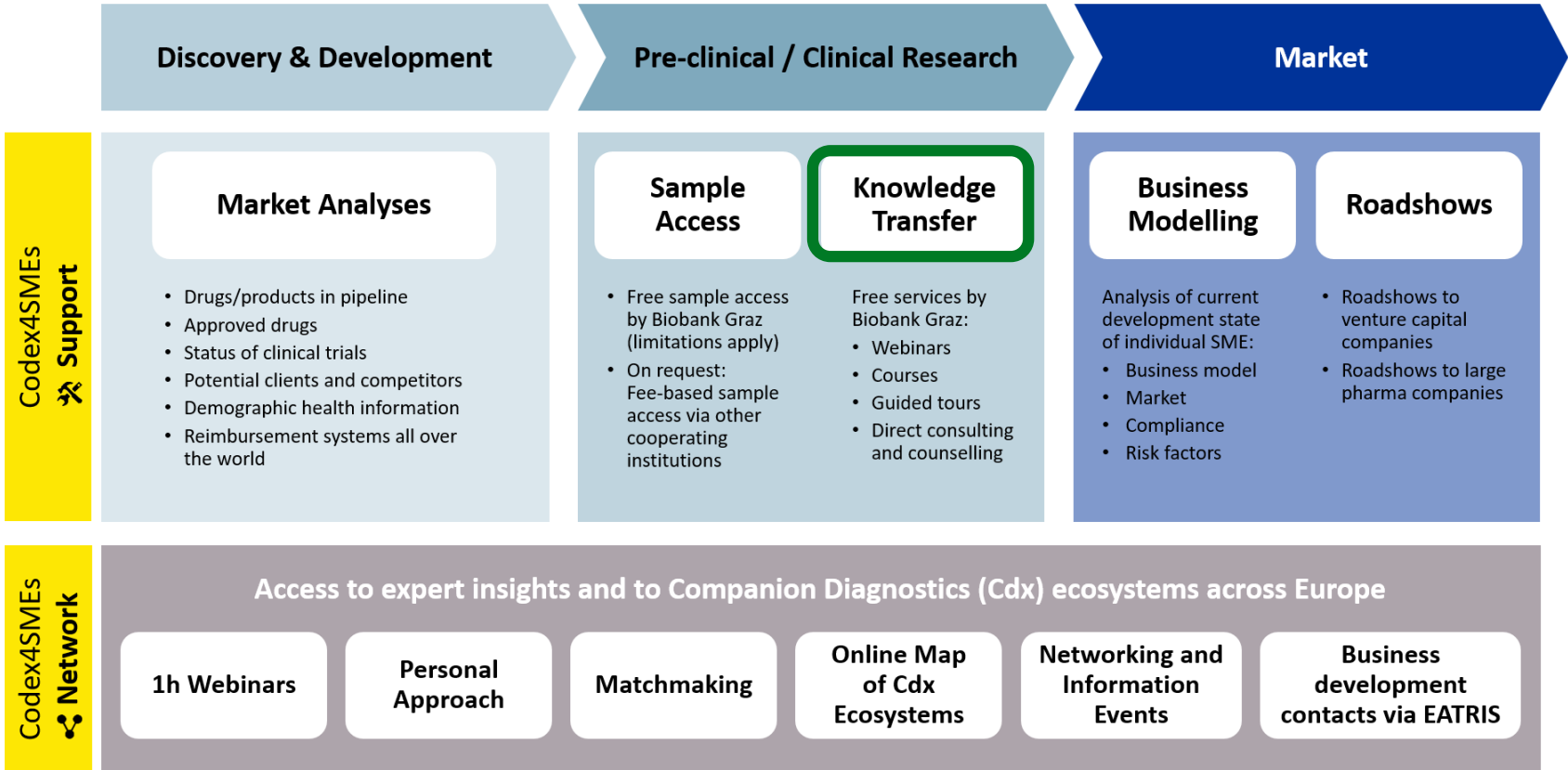
EATRIS European Infrastructure for Translational Medicine, NL



# Codex4SMEs Project - Services

## What is in for you?

Our services for your path towards the market



# Codex4SMEs Project – Free Sample Access Service

to boost your research in the diagnostics' sector

## Samples for Pilot-projects (no ethics vote required)

- ◆ To test or establish a new method
- ◆ Clinical samples from a max. number of **5 patients**

## Samples for Research-projects (valid ethics vote mandatory)

- ◆ Sample access for research projects/biomarker research
- ◆ Clinical samples from a max. number of **20 patients**

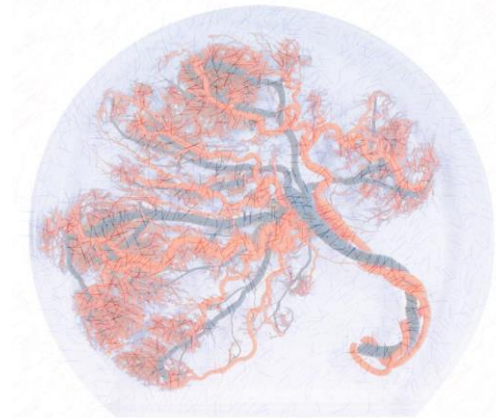
- Open for any European SME working in the Diagnostics' sector
- Samples are provided by the Biobank of Graz
- Ask for sample availability at [codex4smes@medunigraz.at](mailto:codex4smes@medunigraz.at)
- More Info: <https://www.nweurope.eu/codex4smes>

# Biobanking Placental Tissue – Key Aspects of this Organ

Webinar, 4<sup>th</sup> of February, 2021

Pablo Zardoya-Laguardia, PhD

Biobank Graz (Medical University)

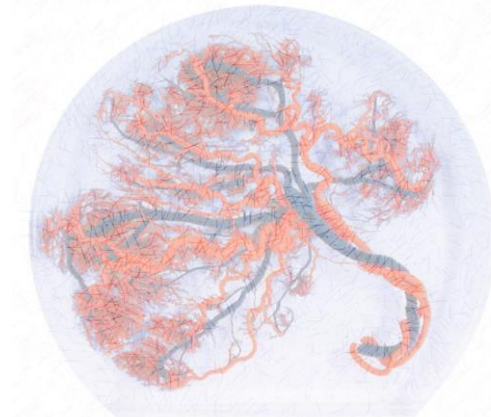


# Biobanking Placental Tissue – Key Aspects of this Organ

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# Biobank

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## Definition

“biorepository that accepts, processes, stores and distributes biospecimens and associated data for use in research and clinical care”

## Goal/Importance

Collect, store and disseminate specimens and related data

Maintenance standards in different processes: collection, processing, storage, tracking and shipment of biospecimens are key to the outcome of a multitude of studies

**Why placenta?**

Yvonne G. De Souza and John S. Greenspan. 2013. Biobanking Past, Present and Future: Responsibilities and Benefits. AIDS. 28; 27(3): 303–312.

# Placenta

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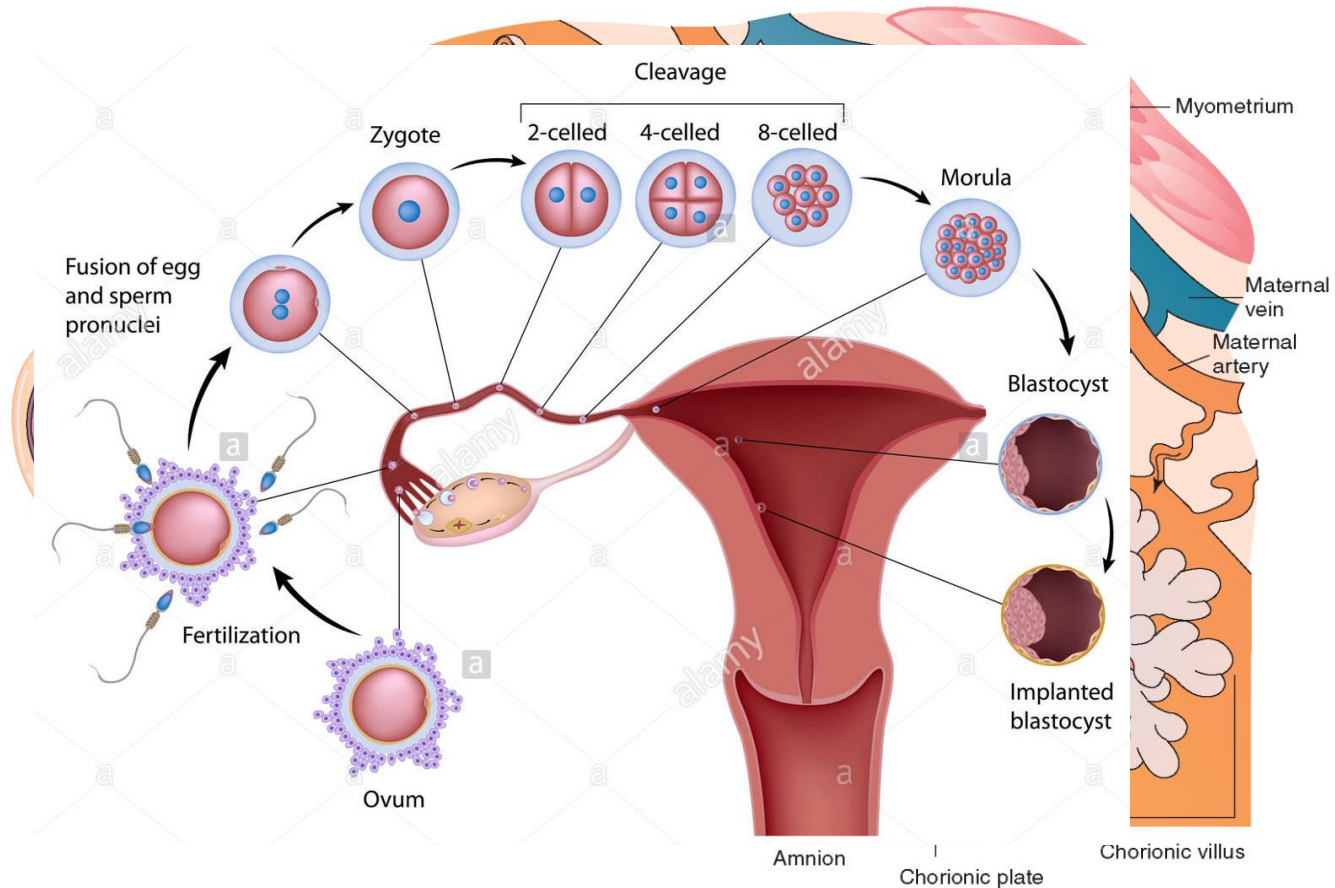
## 1. Historically

- Earliest times → great importance; mysterious/mystical
- Many cultures → alter ego (second self), health & good fortune, talisman (danger)
- Early Egypt → external soul
  - Success/prosperity → well-being of sovereign → bound to preservation of soul
- Pacific islands, Australasia & Africa → sibling of the infant, companion/soul or supernatural properties
- Greeks → importance of placenta for fetal nutrition (chorion and amnion)

Longo, Lawrence & Reynolds, Lawrence. (2009). Some historical aspects of understanding placental development, structure and function. The International journal of developmental biology. 54. 237-55. 10.1387/ijdb.082774ll.

# Placenta

## 2. Development

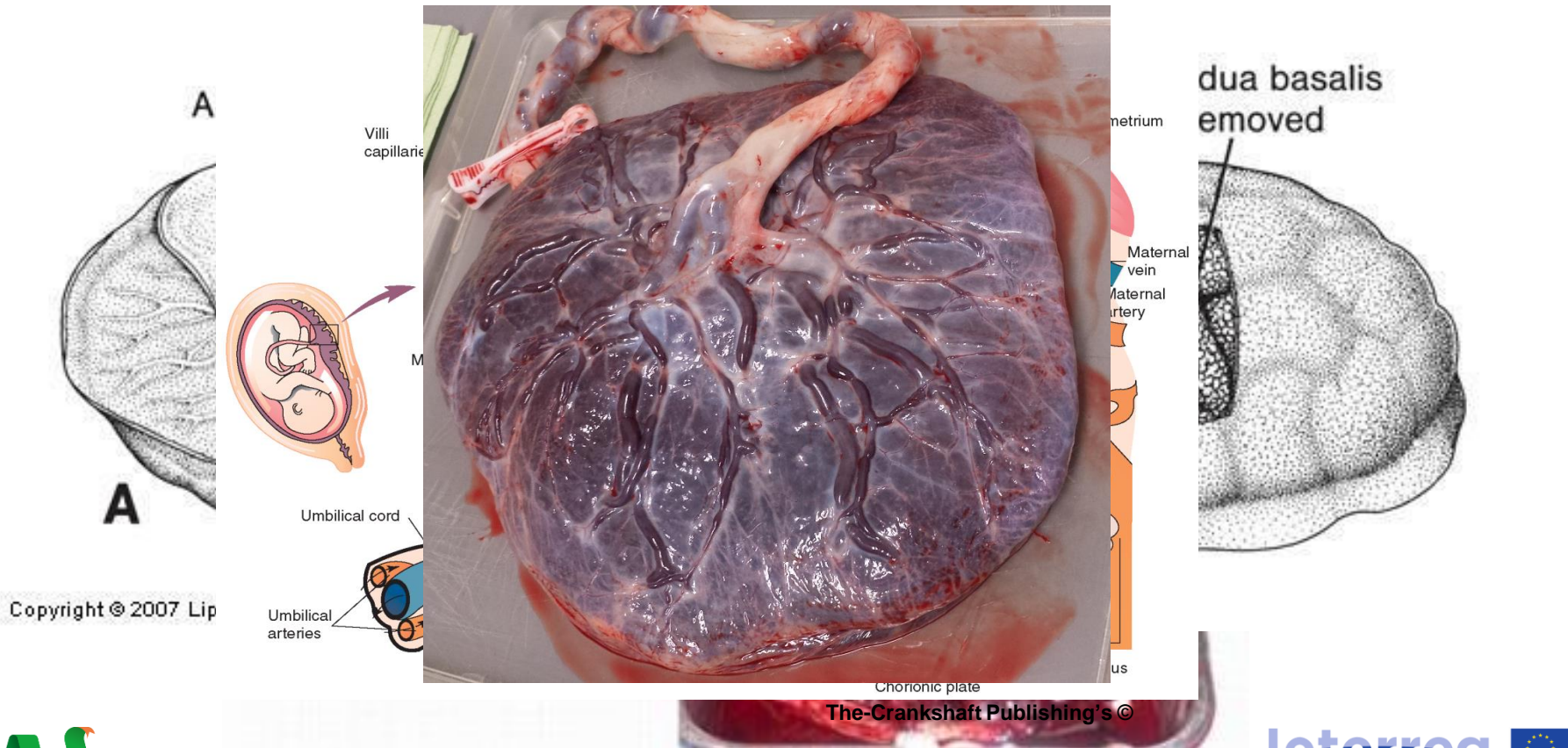


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# Placenta

## 3. Characteristics

- Discoidal organ (~22 cm Ø)



Copyright © 2007 Lip

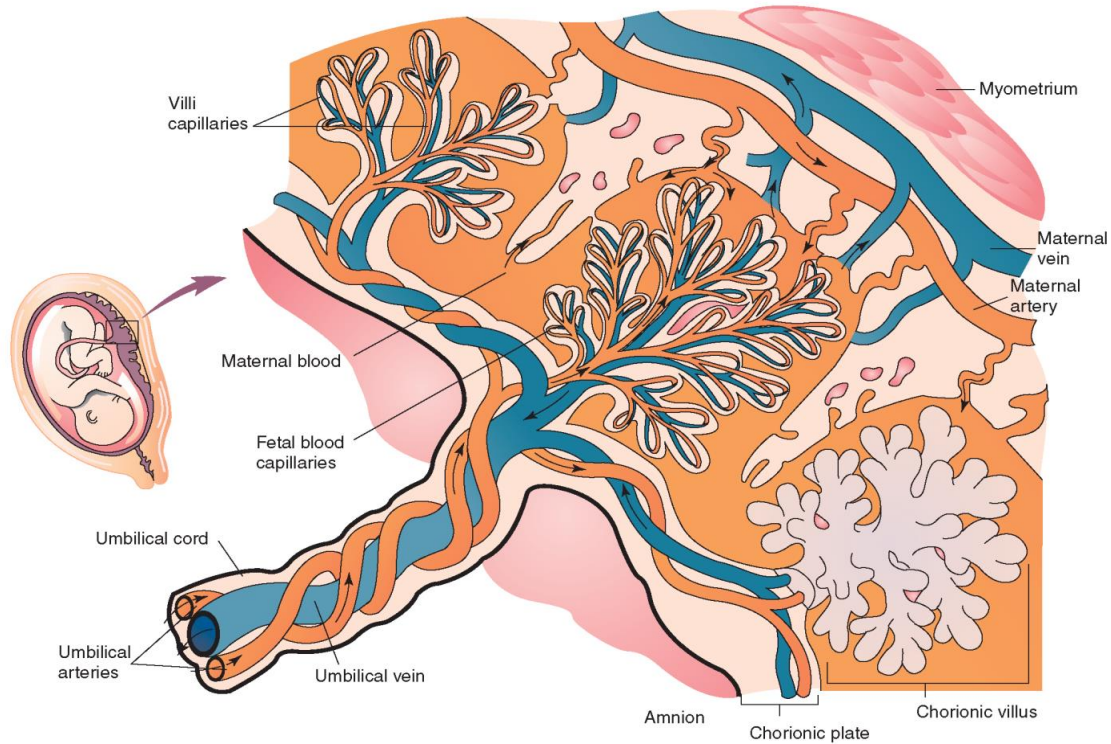
<https://webcampus.drexelmed.edu/neurobio/embryology/page25/page31/>

✉ [codex4smes@medunigraz.at](mailto:codex4smes@medunigraz.at)

# Placenta

## 4. Functions

### A. Gas exchange/nutrient supply



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# Placenta

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## 4. Functions

### B. Hormonal action

- Glucose (Glu) main substrate for placental/fetal metabolism → tight control maternal metabolism → increase maternal Glu and transfer
- Early pregnancy → increased food intake (E storage)
- Term (late pregnancy) → mobilize these reserves for i) fetal growth and ii) lactation
  - ✓ Human placental lactogens (hPL) → increases maternal Glu levels
  - ✓ Placental growth hormone (hGH) → increases maternal Glu levels + enhances fetal growth and placental development
  - ✓ Leptin → increases maternal insulin sensitivity
  - ✓ Strogen, progesterone, relaxin, etc.

## 4. Functions

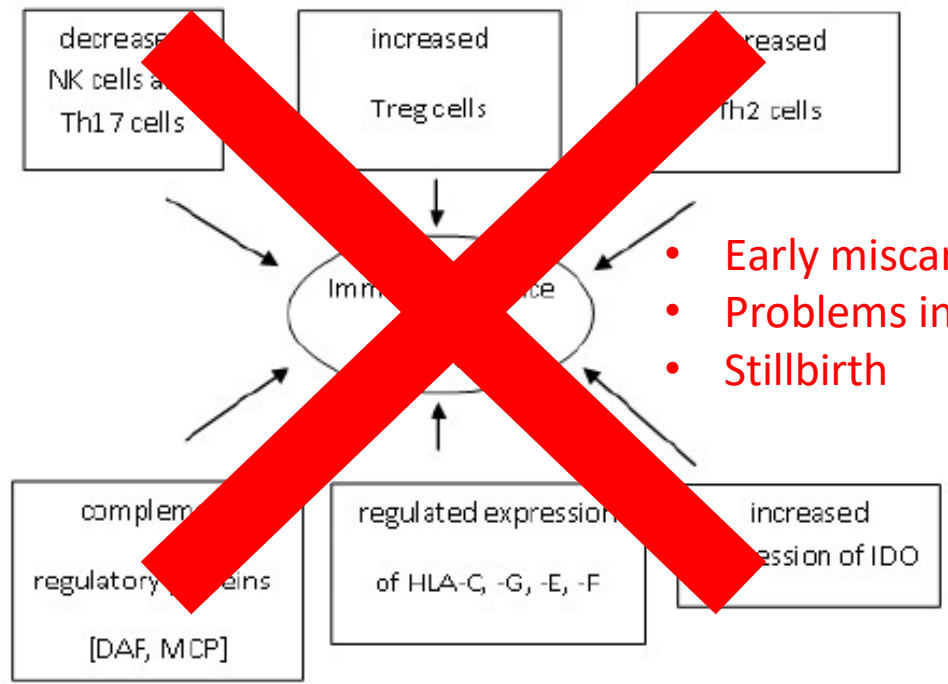
### C. Elimination of metabolites/barrier

- Efflux of waste compounds: urea, uric acid, creatinine, etc.
- Protection against bacteria, drugs or harmful compounds
- Detoxification and efflux of xenobiotics (P-glycoprotein, 11- $\beta$ -hydroxysteroid DH 2, etc)

# Placenta

## 4. Functions

### D. Suppression of the mother's immune system



- Early miscarriage
- Problems in development and growth
- Stillbirth



## 5. Pregnancy complications

### A. Preeclampsia (PE)

- Endothelial dysfunction → hypertension and proteinuria
- Prevention of eclampsia (seizures → coma and death)
- Increases the chances of IUGR

### B. Intrauterine Growth Restriction (IUGR)

- Failure to reach the expected growth potential
- Associated with perinatal mortality + future diseases in child & mother

### C. Preterm birth

- Delivery before the 37<sup>th</sup> week

### D. Gestational Diabetes Mellitus (GDM)

- Impaired Glu tolerance (maladaptation to decreased insulin sensitivity)

Cuffe JSM, Holland O, Salomon C, Rice GE, Perkins AV. Review: Placental derived biomarkers of pregnancy disorders. *Placenta*. 2017 Jun;54:104-110. doi: 10.1016/j.placenta.2017.01.119. Epub 2017 Jan 16. PMID: 28117143

# Placenta

## 6. Traditional Uses

### A. Take home

- Burial → under a tree
- Placentophagy
  - Recipes
  - Pills → steamed, dried, ground into powder & encapsulate → postpartum period (100-200 capsules)
- If not incinerated by hospitals



### B. Industrial

- Cosmetics → hair or skin treatments (extracts animal placenta)
- Pharma → menopause, chronic hepatitis, or osteoporosis (hormone replacement therapy estrogen)
- Food → drinks



# Placenta

## 7. New Uses - Scientific/medical purposes

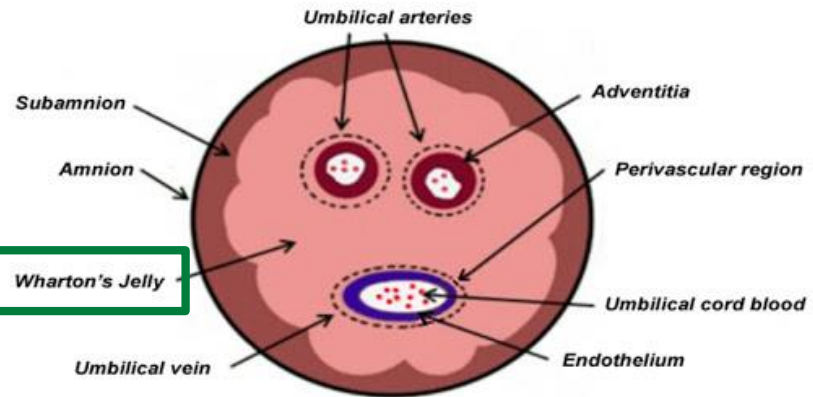
### A. Stem cells

- Amniotic fluid → invasive procedure/decreased efficiency autologous treatment
- Umbilical cord → Wharton's jelly
- Stem cells for autologous & allogeneic therapies
  - Autologous → cord blood banking + annual fees (500-2500\$ once + 100-300\$/year)
  - Allogeneic → 4000-8000\$

### B. Research purposes

#### Mesenchymal Stem Cells:

- ✓ Cartilage
  - ✓ Myocytes/myocytes
  - ✓ Endothelial cells
  - ✓ Retinal progenitor cells
  - ✓ Bone/marrow producing/hepatocytes
  - ✓ Neuroglial cells
- Direct use → institution
- Biobanking



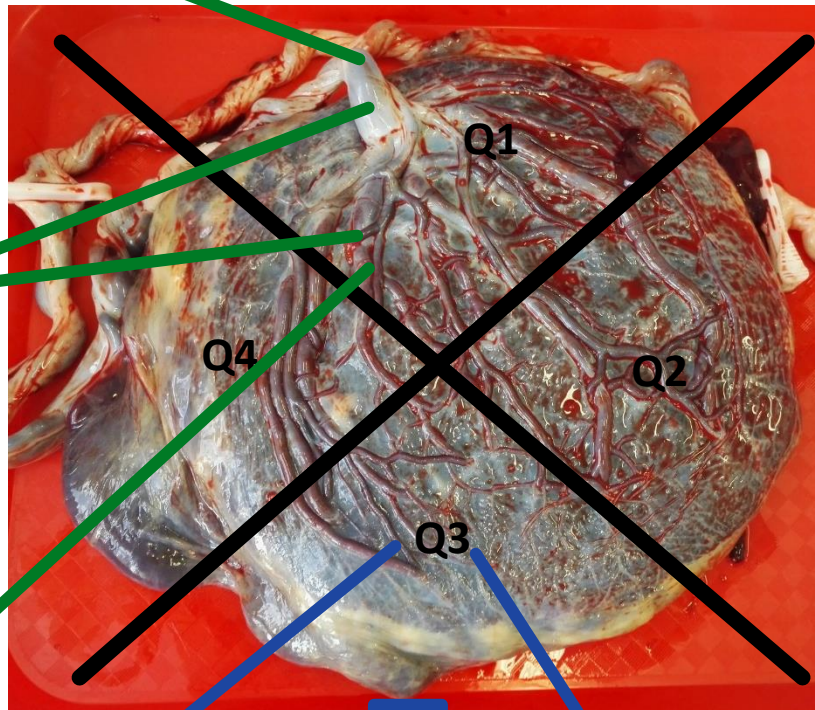
Wang HS, Hung SC, Peng ST, Huang CC, Wei HM, Guo YJ, Fu YS, Lai MC, Chen CC. Mesenchymal stem cells in the Wharton's jelly of the human umbilical cord. *Stem Cells*. 2004;22(7):1330-7. doi: 10.1634/stemcells.2004-0013.

✉ [codex4smes@medunigraz.at](mailto:codex4smes@medunigraz.at)

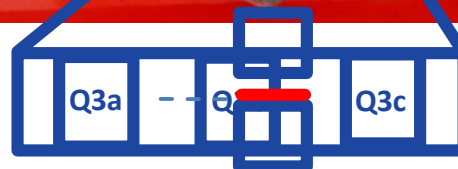
# Biobanking Placental Tissue

## 1. Sample collection

- Artery/vein
- Pieces of tissue
- RNA-later



Q3



# Biobanking Placental Tissue

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## 2. Storage conditions

- Placental tissue → gas phase LN2 ( - 130-140 °C)
- Arteries & Veins → gas phase LN2 ( - 130-140 °C)
- Arterial & Venous Blood → - 80 °C
- RNA-later → - 80 °C

# Biobanking Placental Tissue

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## 3. Factors that can influence subsequent analyses I

### A. Maternal characteristics

- Ethnicity → genetic or epigenetic variations, diet, etc.
- Lifestyle → smoking (decreased vol & capillary surface), alcohol consumption (reduced placental size, reduced flow & impaired transport), etc.
- Body mass index (BMI) → the higher the BMI the smaller the placenta. Obesity related with higher oxidative stress
- Age → placental weight increases with age (maternal and paternal)
- Parity → placental weight is higher in multiparous women
- Medication → diverse effects

### B. Fetal sex

- ✓ Placental weight → placental weights higher/ babies bigger in males
- ✓ Gene expression → different according to sex for maternal inflammatory status

Burton GJ, Sebire NJ, Myatt L, et al. Optimising sample collection for placental research. *Placenta*. 2014 Jan;35(1):9-22. doi: 10.1016/j.placenta.2013.11.005.

# Biobanking Placental Tissue

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## 3. Factors that can influence subsequent analyses II

### C. Mode of delivery

- Vaginal → spontaneous or induced
- Caesarean section → elective or emergency procedure (mech. compression + intermittent reduction of blood supply)
- Other factors → administration of anesthesia (reduced blood flow) or O<sub>2</sub> (higher O<sub>2</sub> concentration), clamping of the cord (early clamping → higher weight)

### D. Interval to sample collection

- Placental weight → the longer the storage the larger the weight loss
- Metabolomics → ATP levels drops after delivery → compromise ATP-dependent activities (ionic pumping)
- Signalling pathways → energy depletion leads to activation of stress pathways
- Gene expression → higher the latter the placenta is collected

Burton GJ, Sebire NJ, Myatt L, et al. Optimising sample collection for placental research. *Placenta*. 2014 Jan;35(1):9-22. doi: 10.1016/j.placenta.2013.11.005.

# Biobanking Placental Tissue

## 4. Biomarkers

- Passive biomarkers → by-products of placental processes
  - Protein carbonyls → increased in maternal serum of PE, IUGR, GDM and preterm birth
  - Oxidised DNA → increased in maternal urine of IUGR and GDM
  - Heat shock protein 70 → increased in maternal serum of PE and preterm birth
  - Placental vesicles → increased in maternal serum of PE and GDM
  - Mitochondrial DNA (mtDNA) → increased in maternal blood of PE and IUGR
- Bioactive molecules → regulate maternal physiology
  - Ratio soluble fms-like tyrosine kinase-1 (sFLT1)/Placental growth factor (PGF) → PE
  - Soluble endoglin (sENG) → increased in maternal serum of PE and other complications
  - Pregnancy-specific glycoprotein 1 (PSG1) → glycosylated levels higher in GDM

Manokhina I, Del Gobbo GF, Konwar C, Wilson SL, Robinson WP. Review: placental biomarkers for assessing fetal health. Hum Mol Genet. 2017 Oct 1;26(R2):R237-R245. doi: 10.1093/hmg/ddx210. PMID: 28595268.

Cuffe JSM, Holland O, Salomon C, Rice GE, Perkins AV. Review: Placental derived biomarkers of pregnancy disorders. Placenta. 2017 Jun;54:104-110. doi: 10.1016/j.placenta.2017.01.119. Epub 2017 Jan 16. PMID: 28117143



# Biobanking Placental Tissue

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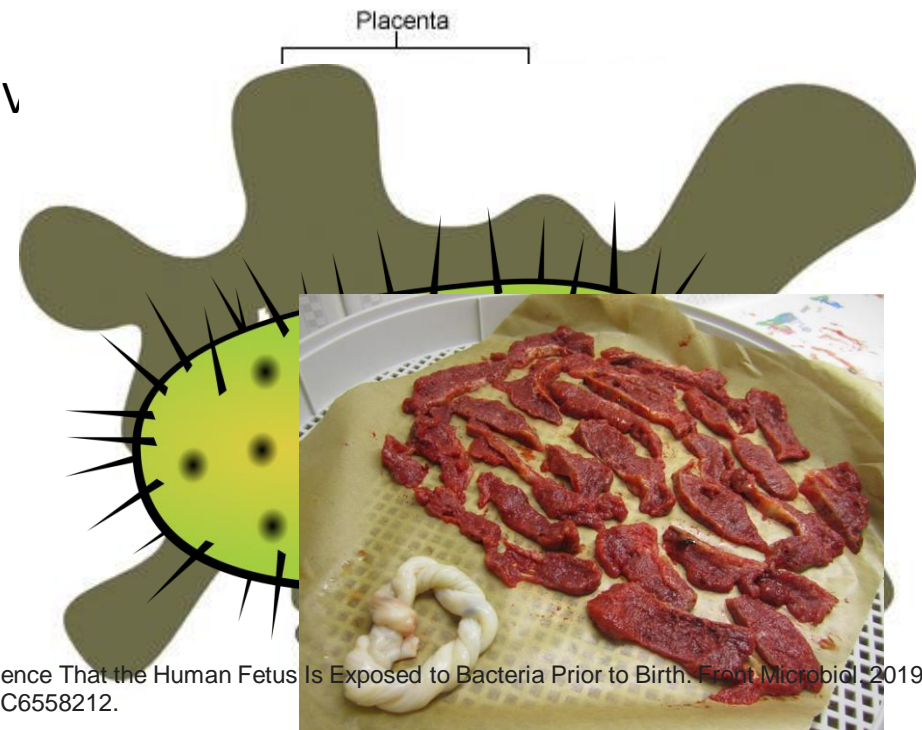
## 5. Research relevance

- Identifying placental processes and medical treatments that lead to adverse pregnancy outcomes for the mother & newborn (PE, IUGR, GDM, preterm birth, etc.)
- Identify potential pathways and the best times in early and late pregnancy to use medication to avoid placenta-related problems
- The placenta's role in future disease in mother and child
- Reduce maternal and fetal morbidity and mortality

# Curiosities

## Curiosities

1. Umbilical Cord → 2 Arteries & 1 V
2. Meconium
3. Placenta Sterile?
4. Placentophagy/placentophagia



Stinson LF, Boyce MC, Payne MS, Keelan JA. The Not-so-Sterile Womb: Evidence That the Human Fetus Is Exposed to Bacteria Prior to Birth. *Front Microbiol*. 2019 Jun 4;10:1124. doi: 10.3389/fmicb.2019.01124. PMID: 31231319; PMCID: PMC6558212.

Marraccini ME, Gorman KS. Exploring Placentophagy in Humans: Problems and Recommendations. *J Midwifery Womens Health*. 2015 Jul-Aug;60(4):371-9. doi: 10.1111/jmwh.12309. PMID: 26255799.

Farr A, Chervenak FA, McCullough LB, Baergen RN, Grünebaum A. Human placentophagy: a review. *Am J Obstet Gynecol*. 2018 Apr;218(4):401.e1-401.e11. doi: 10.1016/j.ajog.2017.08.016. Epub 2017 Aug 30. PMID: 28859955.

# Thank You !

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Biobank Graz Team

Bettina Antmann



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# Questions?

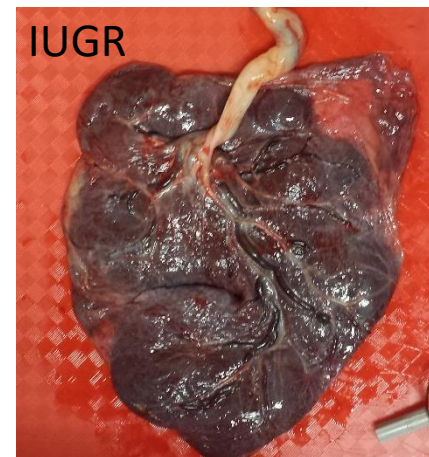
1. XXX

# Additional Info

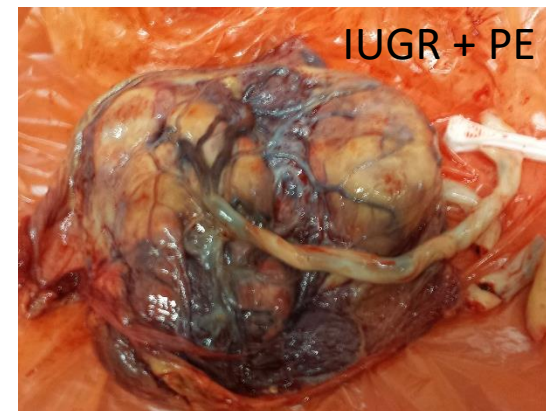
Normal



IUGR



IUGR + PE



# Biobanking Placental Tissue

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## 5. Clinical relevance (macroscopically)

- Placental completeness → retained placental tissue associated with haemorrhage and infection
- Placental size → < 2.5 cm thick IUGR or > 4 cm thick Diabetes/fetal hydrops
- Placental shape → postpartum infection & haemorrhage
- Placental consistency and surfaces → fetal anemia or hemorrhage
- Umbilical cord (length, insertion, diameter and inflammation) → malformations

Yetter JF 3rd. Examination of the placenta. Am Fam Physician. 1998 Mar 1;57(5):1045-54. PMID: 9518951.

# Additional Info

## Placental products used as medicine and cosmetics

Product name	Manufacturer	Country	Clinical application	Administration
Placentrex	M/s Albert David	India	Wound healing	Intramuscular injection, topical gel and lotion
Laennac	Japan Bioproducts Industry	Japan	Hepatoprotection, skin rejuvenation and whitening	Intramuscular injection
Melsmon Cell Revitalization Extract	Melsmon Pharmaceuticals	Japan	Cell revitalisation and promoting neoangiogenesis	Intramuscular injection
MF II	-	Switzerland	Cellular regeneration and tissue healing	Intramuscular injection and capsules for oral intake
Placenta ampoule	DIO International	Korea	Skin renewal	Intramuscular injection
Sheep Placenta	Deep Blue Health	New Zealand	Dietary food supplement	Capsules for oral intake
Sheep Placenta	Careline Group Pty.	Australia	Anti-aging, skin revitalization, allergy resistance	Capsules for oral intake, skin cream for topical use
Sheep Placenta Soft Gel	Guangzhou Boan Health Products	China	Nutritional supplement	Capsules for oral intake
Sheep Placenta Extract Powder	Anzchem Pty.	Australia	Promote cell growth, hormone regulation and skin hydration	Water soluble powder suitable for manufacture of capsules, lotions and creams
Lamb Placenta Soft Capsules	Guangdong Luck-sun Medicine	China	Skin rejuvenation and nutritional supplement	Capsules for oral intake
Placenta Hydrolysate	Hangzhou Huajin Pharma	China	Stimulates proliferation of hepatocytes	—
Sheep Placenta Extract	Youzhiyou Biotechnology	China	Skin regeneration and whitening factor	For topical use



# Additional Info

## Placental products used as medicine and cosmetics

Larins Placenta Cream	Untouched Native	New Zealand	Rejuvenation of the skin, and protection from environmental damage and scar reduction	Skin cream for topical use
Regenerating Active	Nelson Laboratory	New Zealand	Rejuvenation of the skin	Topical skin cream and eye serum
Placenta BB cream	Dermal Korea	Korea	Blemish balm for sensitive skin	Skin cream for topical use
Gold Rejuvenating Placental Serum	Ecowool	New Zealand	Anti-ageing	Skin serum for topical use
Placenta range	Lanocrema	New Zealand	Cell renewal, improve skin elasticity and skin nourishment	Skin cream and lotion for topical use
EMK Placental Skin Care Products	EMK Products, LLC	US	Anti-ageing, and skin and hair rejuvenation	Skin cream, lotion, serum and injections