

Quorum sensing peptides: missing link between microbiome and health?

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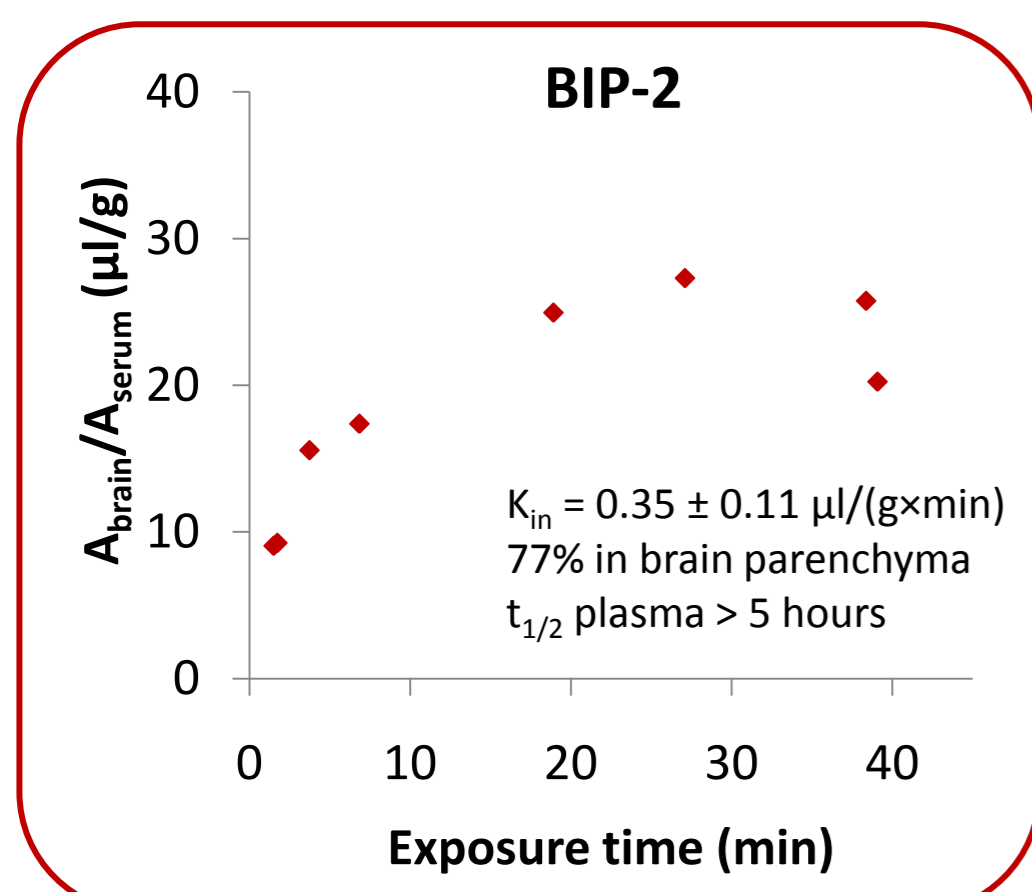
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INTRODUCTION & OBJECTIVES

The human microbiota is currently being investigated for their role in tumorigenesis. However, while current research mainly focuses on toxin production or reactive oxygen or nitrogen species (ROS/RNS) formation, the role of quorum sensing peptides is not yet investigated.

Therefore, our research explores the influence of quorum sensing peptides (QSP) (<http://quorumpeps.ugent.be>) [1] on cancer cells as well as their initial pharmacokinetic properties.

RESULTS

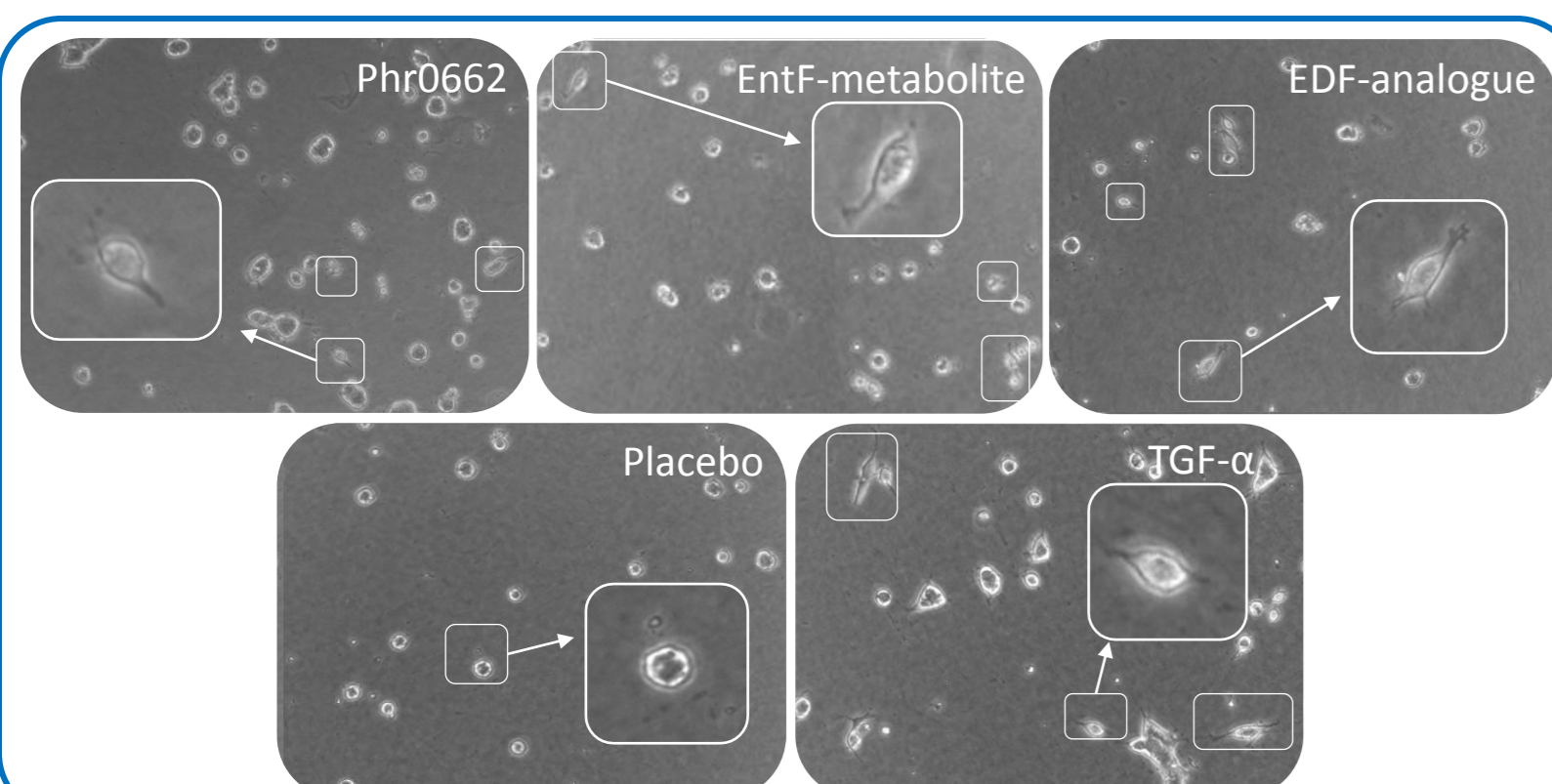


BBB penetration

Methods: *In vivo* (mice) multiple time regression (MTR), efflux, capillary depletion (CD) and human plasma/brain stability studies.

Quorum sensing peptides can cross the blood-brain barrier (BIP-2: *Streptococcus pneumoniae*)

→ LINK WITH CENTRAL NERVOUS SYSTEM DISORDERS?

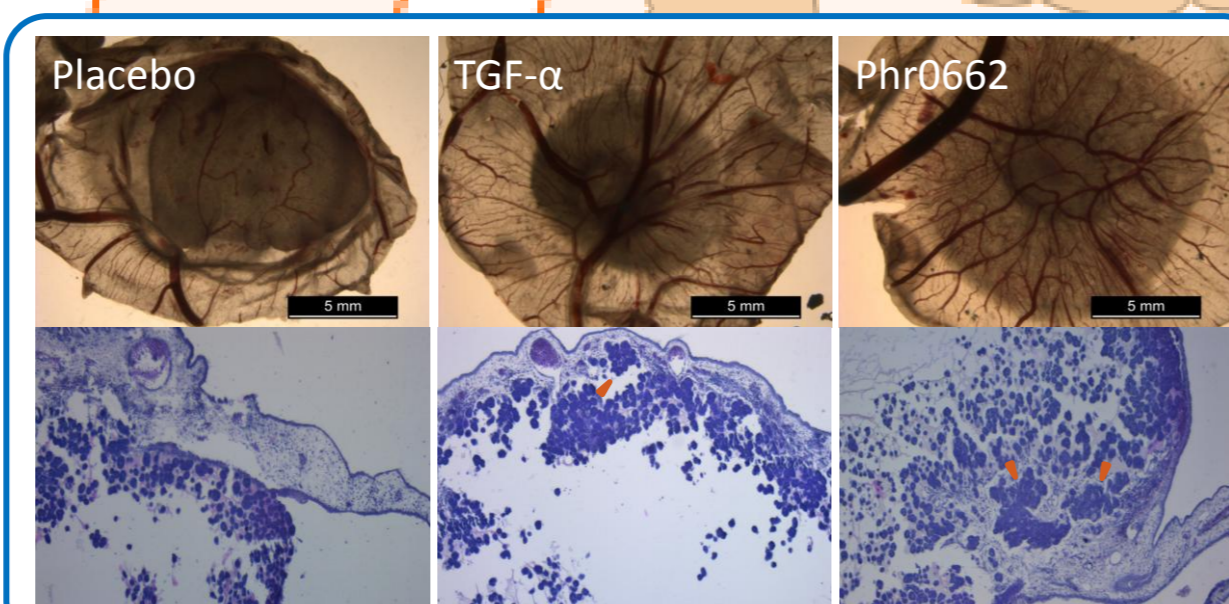


Peptide	Origin
Phr0662 (ERNNT)	<i>Bacillus</i> spp.
EntF-metabolite (SNLVECVFSLFKKCN)	<i>Enterococcus faecium</i>
EDF-analogue (NWN)	Derived from <i>Escherichia coli</i>

Cell medium half-life: > 18 hours (all)

Colon cancer

Methods: collagen type I invasion, transcriptome profiling, Chick Chorioallantoic Membrane (CAM), cytokine expression, phospho-receptor tyrosine kinase array and cell medium stability assays.



Some (other) quorum sensing peptides promote colon cancer (HCT-8/E11) cell invasion/migration and angiogenesis (both *in vitro* and *in vivo*)

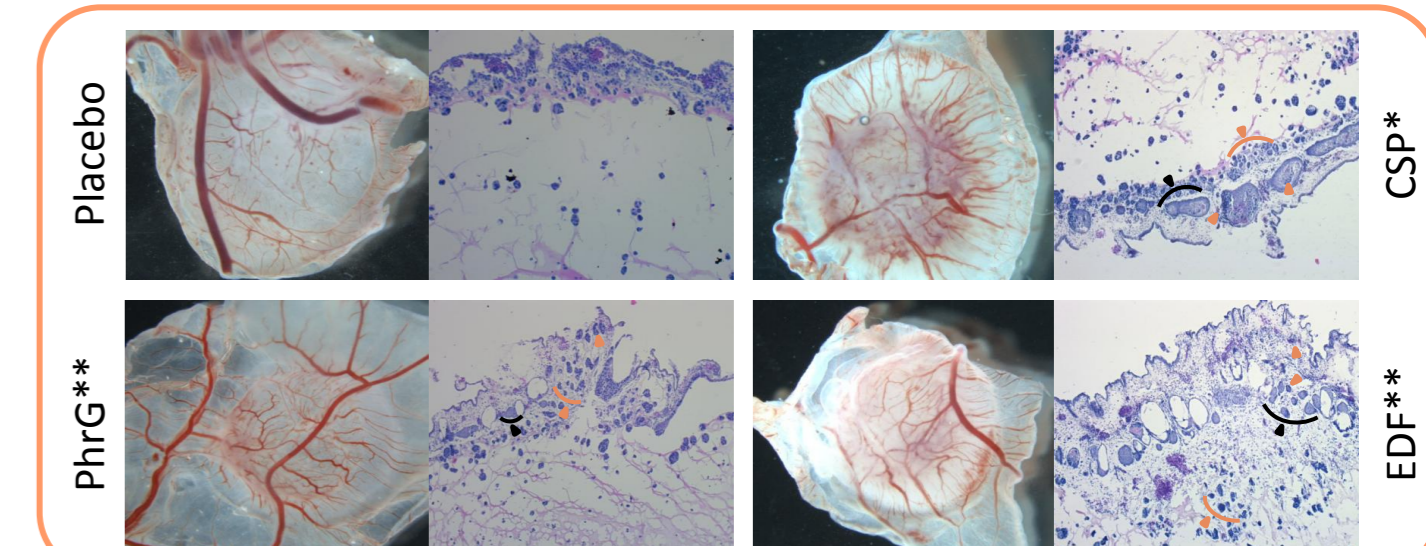
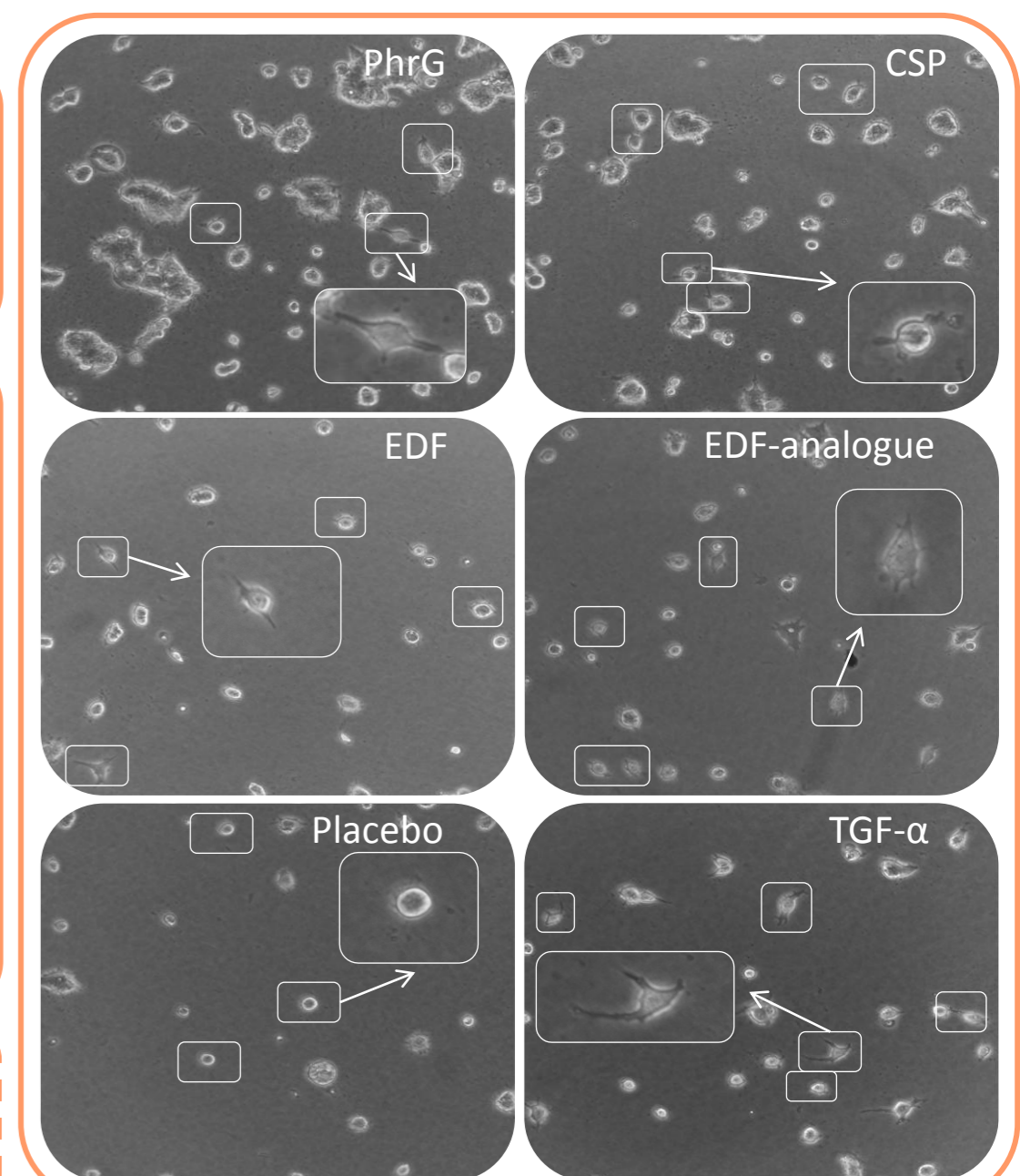
→ CANCER METASTASIS

Breast cancer

Methods: collagen type I invasion, transcriptome profiling, Chick Chorioallantoic Membrane (CAM), protein expression and cell medium stability assays.

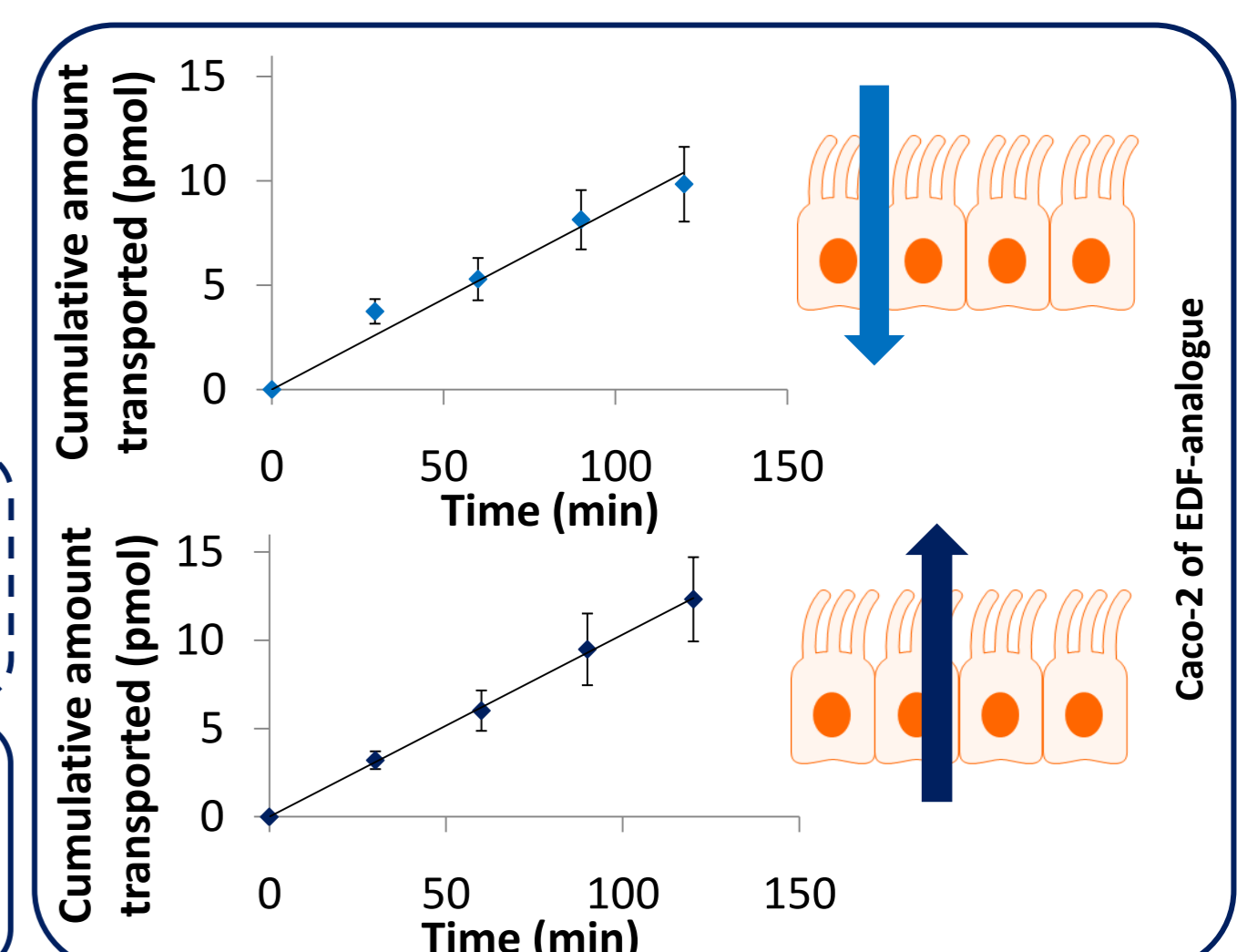
Peptide	Origin
PhrG (EKMIG)	<i>Bacillus subtilis</i>
CSP (EMRKSNNFFHFLRRI)	<i>Streptococcus mitis</i>
EDF (NNWNN)	<i>Escherichia coli</i>
EDF-analogue (NWN)	Derived from <i>Escherichia coli</i>

Cell medium half-life: > 16 hours (all)



Some quorum sensing peptides significantly promote breast cancer (MCF-7/AZ) cell invasion/migration (EMT) (*in vitro*) and angiogenesis (*in vivo*)

→ CANCER METASTASIS



Some quorum sensing peptides can pass the intestinal barrier (Caco-2 cell) and reach the blood circulation

→ EFFECT AT DISTANT SITES OF THE BODY

Intestinal permeability

Methods: Caco-2 transport studies and HPLC/ESI-MS quantification.

Quorum sensing peptides induce (breast and colon) cancer cell invasion and angiogenesis, thereby potentially influencing cancer metastasis. Moreover, due to their permeability through the blood-brain barrier, these peptides can affect the central nervous system as well, including brain cancers. Our results thus indicate that an adaptation of the patient's life style (e.g. food consumption, hygiene) can influence cancer outcome through quorum sensing peptides crosstalk.

CONCLUSIONS

REFERENCES

[1] Wynendaele E, *et al.* Quorumpeps database: chemical space, microbial origin and functionality of quorum sensing peptides. *Nucleic Acids Research* 2013, 41, D655-D659.