Effect of immune responses on breath methane dynamics

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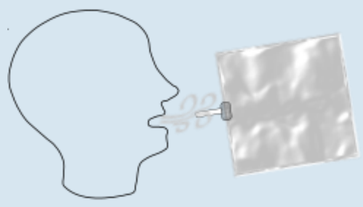
STATE OF KNOWLEDGE

- breath CH_4 exclusively reflects microbial activity in the gut
- increased methane production might be linked to specific colonic disorders
- variation in breath CH_4 might be linked to changes in colonic transit time
- probability of increased breath CH_4 (> 3 ppmv) increases with age[1]
- recently, first indications that CH_4 could also be formed endogenously in cells through oxidative-reductive stress reactions[2]

CH_4 MEASUREMENT



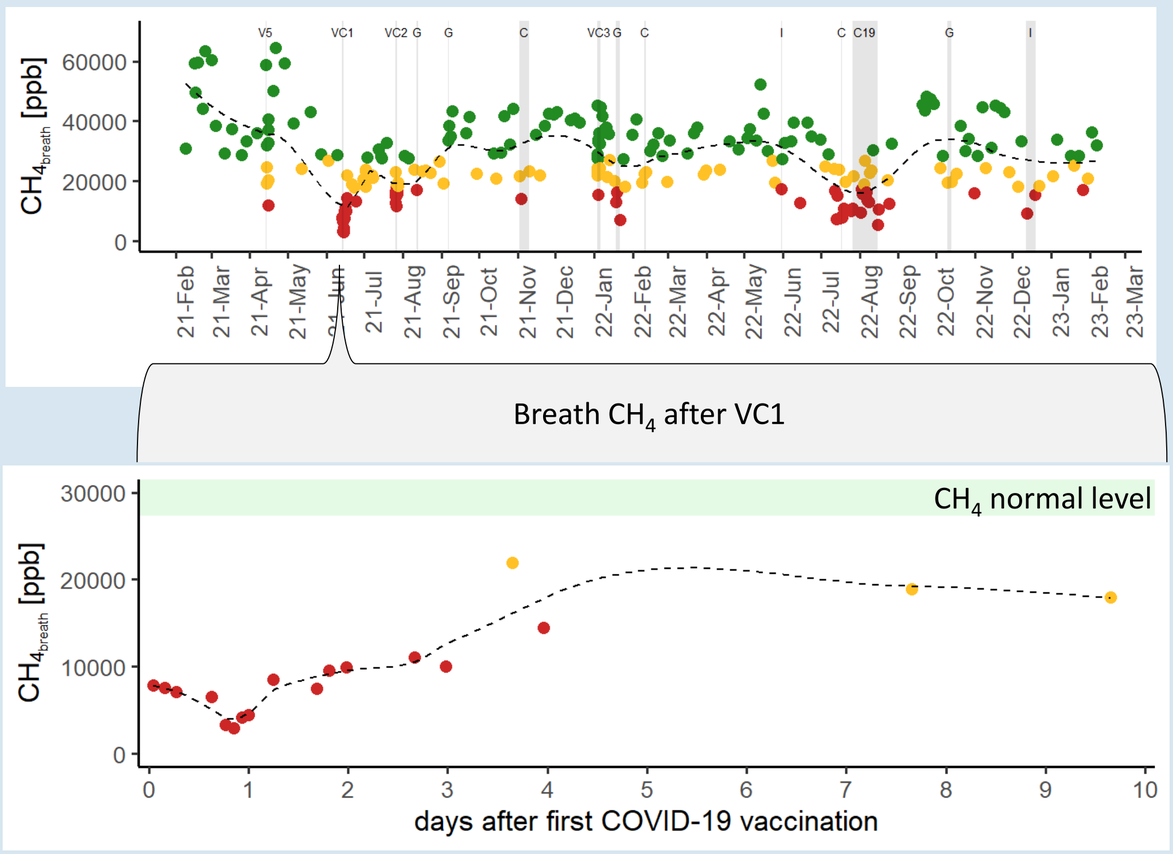
- breath CH_4 was measured by gas chromatograph coupled to a flame ionization detector with an analytical precision of 0.1 ppmv
- Stable isotope values of breath CH_4 ($\delta^{13}C$ and $\delta^{2}H$) were measured by an isotopic ratio mass spectrometer with an analytical precision of 0.3 mU for $\delta^{13}C$ and 3 mU for $\delta^{2}H$

LONG-TERM MONITORING OF BREATH CH_4 IN TWO SUBJECTS

subject A

female; 45 yrs

index	event	symptoms
C	common cold	rhinorrhea, cough, sore throat
G	gastrointestinal complaints	constipation
I	mild inflammation	hidradenitis suppurativa
V5	vaccination: diptherie, pertussis, tetanus, Polio, FSME	no symptoms
VC 1-3	Covid-19 vaccinations (Moderna)	limb pain, increased temperature
C19	Covid-19 infection	limb pain, headache, sore throat



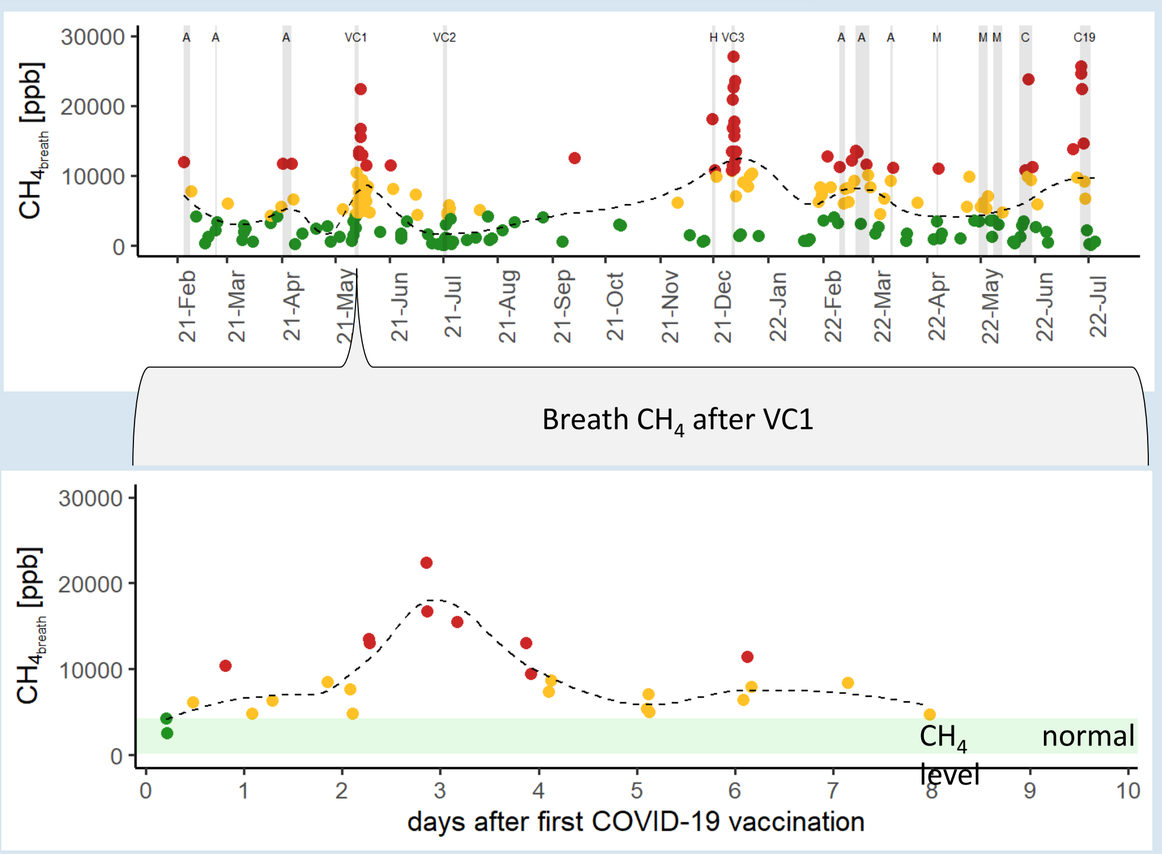
Breath CH_4 after VC1

⇒ CH_4 level **decreases** during immune reactions

subject B

male; 55 yrs

index	event	symptoms
A	allergic rhinitis	rhinorrhea, conjunctival swelling
H	headache	migrainous headache without aura
M	muscle ache	strong muscle ache after pronounced physical exercise
C	common cold	rhinorrhea, cough, sore throat
VC 1-3	Covid-19 vaccinations (Biontech)	limb pain, headache
C19	Covid-19 infection	limb pain, headache, sore throat



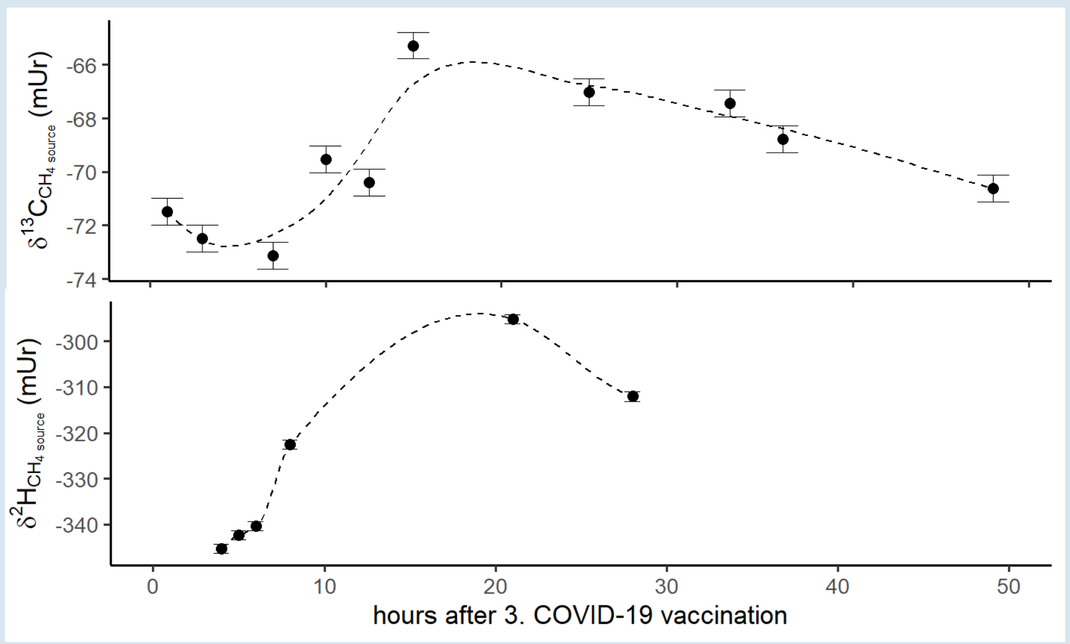
Breath CH_4 after VC1

⇒ CH_4 level **increases** during immune reactions

REDUCED CH_4 PRODUCTION OR CH_4 DEGRADATION?

Tool to disentangle the present process : stable isotopes of CH_4

⇒ **$\delta^{13}C$ and $\delta^{2}H$**

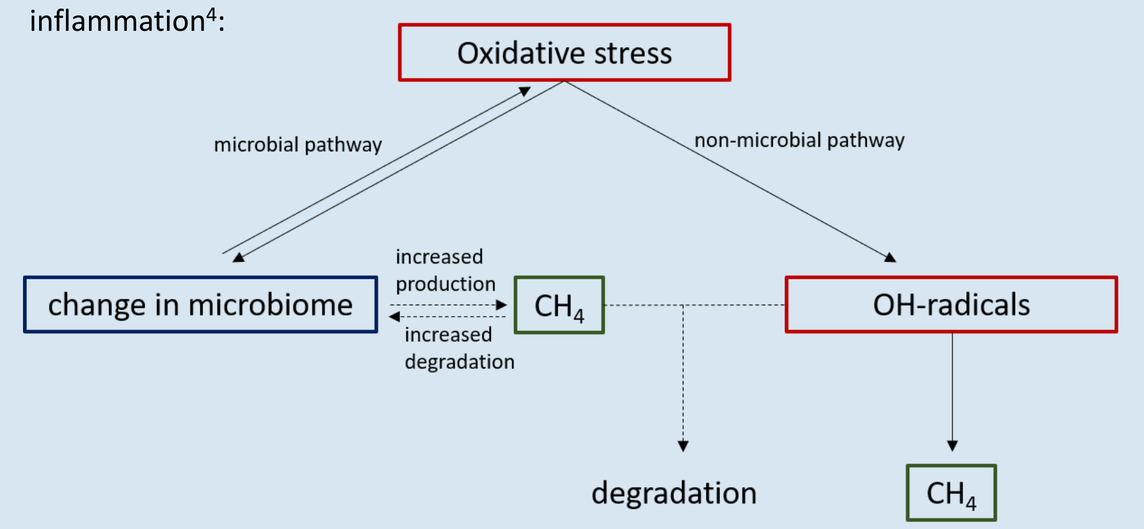


⇒ increase in stable isotopes of CH_4 after vaccination (induced perturbation of the immune system) supports the hypothesis of enhanced **CH_4 degradation**

CONCLUSION

CH_4 is a bioindicator for **general immune reactions**[3]

scheme of hypothetic microbial and non-microbial pathways of CH_4 production and CH_4 degradation triggered by oxidative stress during inflammation[4]:



OUTLOOK

- clinical trial to monitor breath CH_4 in a large number of subjects, including the study of immune parameters and microbial composition
- specific stable isotope studies to identify precursors and degradation products of CH_4 to elucidate CH_4 pathways (microbial and non-microbial) in the human body

⇒ Investigation of the bioactive role of breath CH_4 to classify immune responses, e.g., with respect to vaccine efficacy

[1]**Polag, D**., Leiß, O., & **Keppler, F.** (2014). Age dependent breath methane in the German population. *Science of the Total Environment*, 481, 582-587.
[2]**Keppler, F.,** Boros, M., & **Polag, D.** (2023). Radical-driven methane formation in humans evidenced by exogenous isotope-labeled DMSO and methionine. *Antioxidants,* 12.
[3]**Polag, D**. & **Keppler, F.** (2023). Effect of immune responses on breath methane dynamics. *Journal of Breath Research*.
[4]Ernst, L., Steinfeld, B., Barayeu, U., Klintzsch, T., Kurth, M., Grimm, D., . .& **Keppler, F.** (2022). Methane formation driven by reactive oxygen species across all living organisms. *Nature,* 603, 482–487.

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