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Methionine Addiction: The Fundamental Hallmark of Cancer

Dr. Robert M. Hoffman

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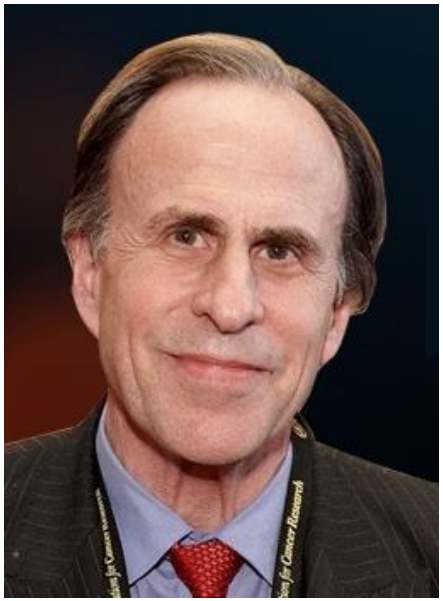
About the Speaker



Dr. Robert Hoffman

- President, Chairman of Board and CEO at AntiCancer, Inc.
- Professor in the Department of Surgery at the University of California, San Diego
- Veteran scientist with 55+ years of experience in cancer research, 1100+ publications and 52283 citations
- Editorial Board member of Clinical Cancer Research, Journal of Fluorescence Guided Surgery, In Vitro Cellular and Developmental Biology, and Anticancer Research

Agenda

AGENDA

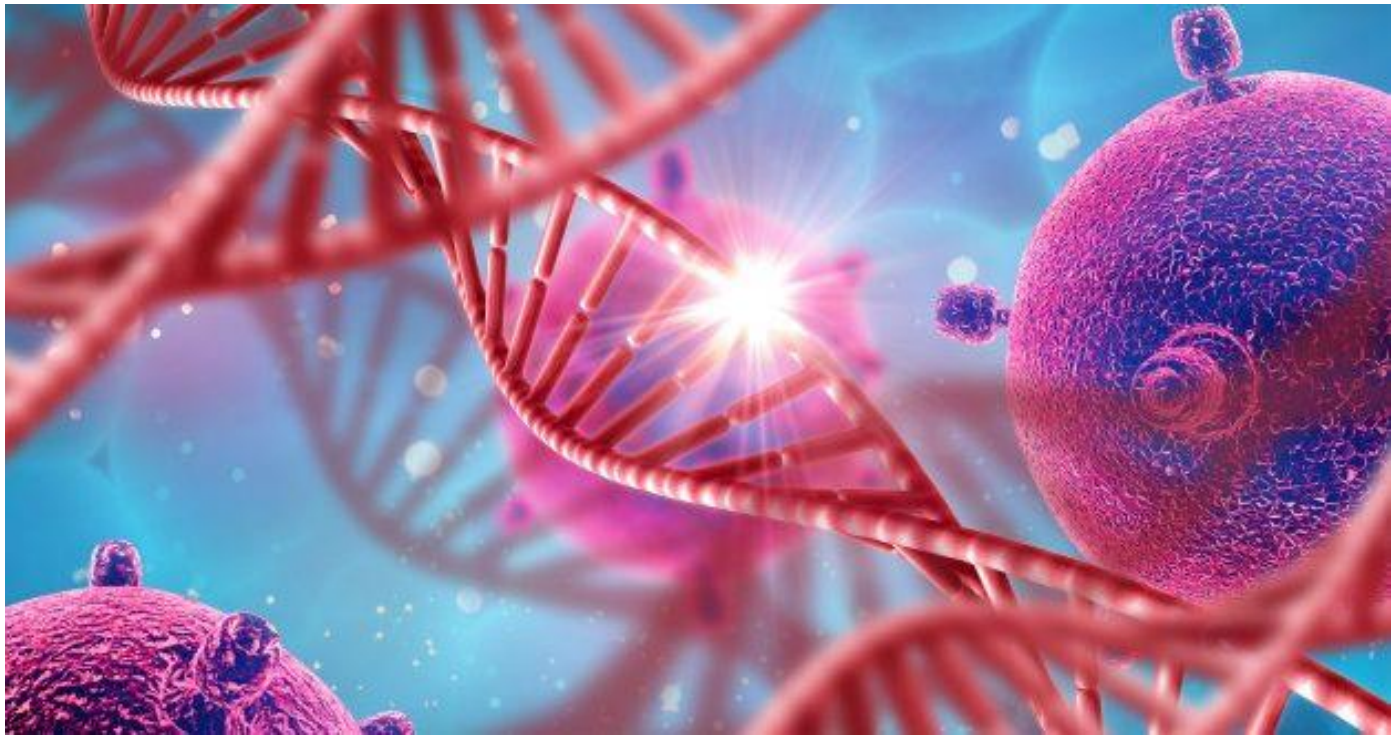
Source: European Pharmaceutical Review

1	Introduction to the Hoffman effect – Methionine Addiction of Cancer
2	Role of Methylation and Transmethylation Reactions
3	Methionine Addiction as a Pan-Cancer Therapeutic
4	Future of Cancer Research

Introduction to the Hoffman Effect – Methionine Addiction of Cancer

Paradigm of Cancer Research

Status of Cancer Research in Early 1970s – When Methionine Addiction was Discovered by Dr. Hoffman



Methionine Dependence of Cancer

Evidence from cancer-based studies:

(Sugimura and colleagues, 1959)
Experiment – Tumor-bearing rats fed with amino acid restricted diets
Observation – Tumor growth and proliferation significantly affected by ***methionine-restricted diet.***

(Chello and colleagues, 1973)
Experiment – Growth characteristics of Leukemia cells supplemented with methionine and homocysteine
Observation – Leukemia cells ***failed to proliferate in growth media where methionine was substituted*** with its metabolic precursor, ***homocysteine.***

Methionine Addiction Mechanism

Addiction of cancer cells to exogenously provided methionine is not due to their failure to synthesize methionine from homocysteine but is due to **an increased demand for trans-methylation by cancer cells**

'Hoffman effect'

Source: A*Star Research

Role of Transmethylation

Histones- The Methyl Addicts

Methionine addiction is the fundamental and general hallmark of cancer!

Overuse of methionine – METHIONINE ADDICTION- results from cancer cells performing excessive transmethylation reactions

"Over-methylation of ***histone H3 lysine*** is necessary for methionine addiction of cancer- thereby promoting MALIGNANCY"

PET Imaging

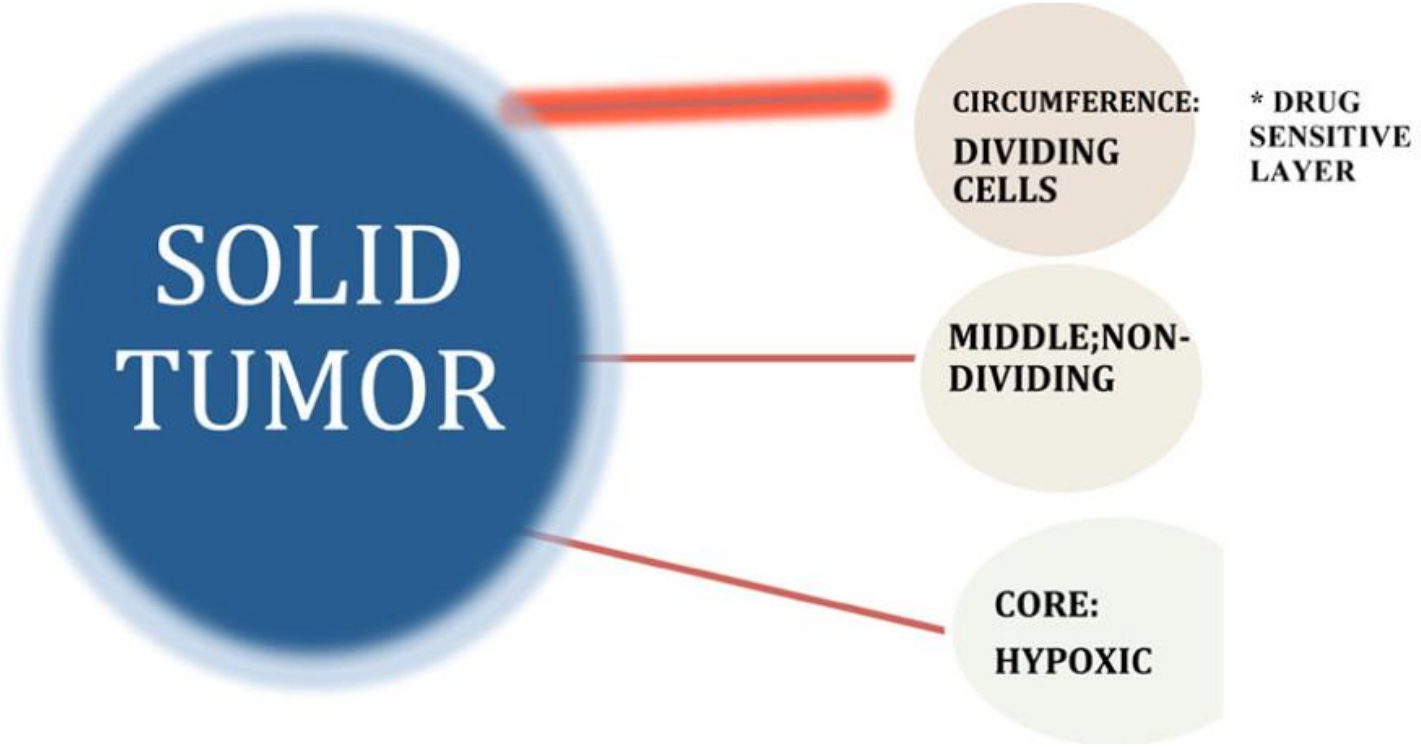
PET imaging of cancer with [C^{11}] methionine in the clinic gives a stronger signal than [^{18}F] deoxyglocose showing that

"**Hoffman effect is stronger than the Warburg effect**"

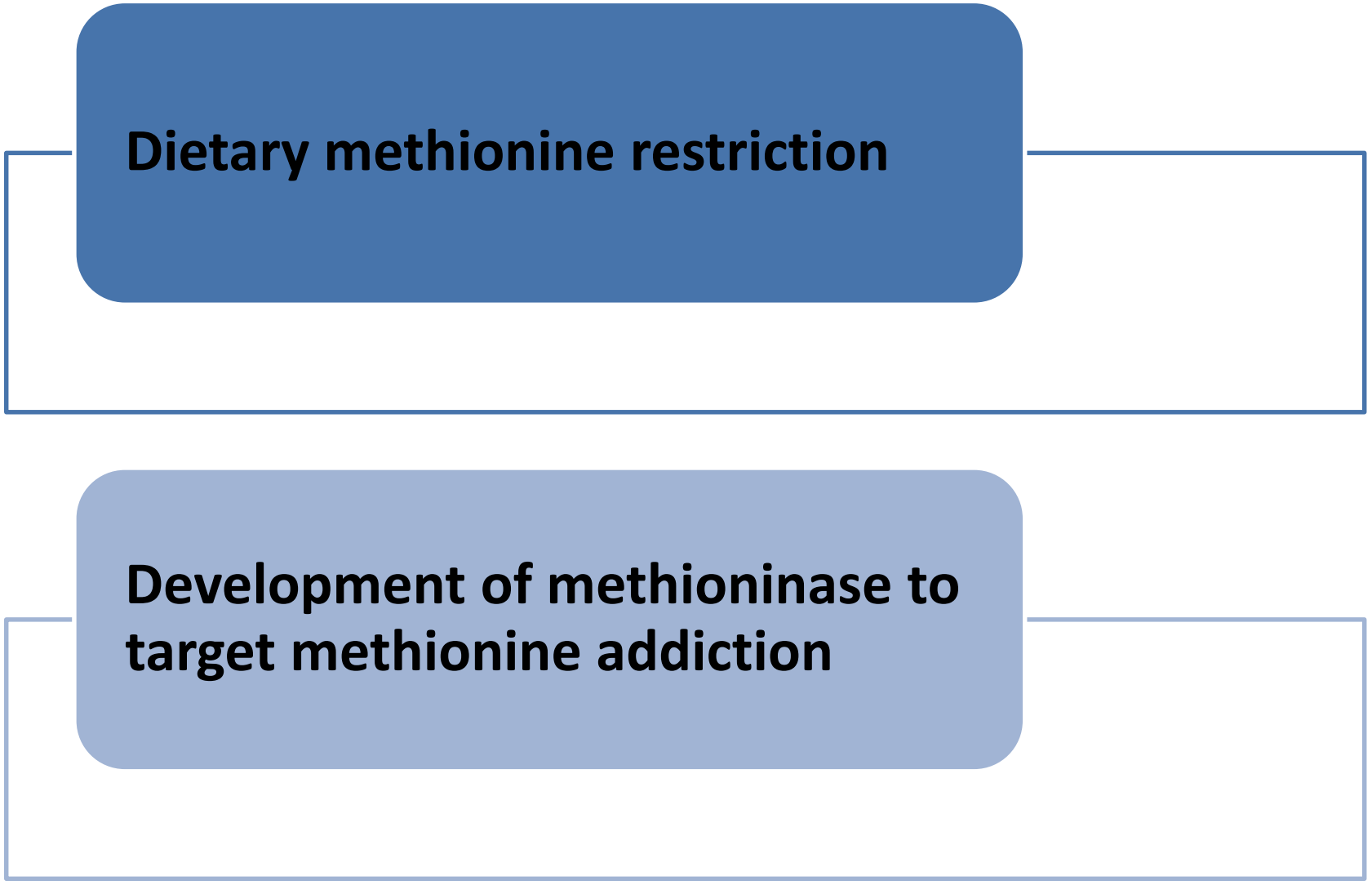
Methionine Addiction as a Pan-Cancer Therapeutic

Limitations of Chemotherapy

Cancer patients with ***solid tumors*** do not respond to drugs effectively as the cells in their tumors are mostly ***non-dividing***, and therefore ***resistant to drugs***.
They must be treated differently!



Novel Therapeutic Approaches



Dietary Methionine Restriction

- Dietary methionine restriction has shown some promising results - significantly suppress tumor growth in multiple models including both solid tumors and blood cancers. However, patients cannot tolerate well the methionine-restricted diets.
- Methionine restriction may synergistically enhance response to chemotherapy
- Combination of methionine restriction and 5-fluorouracil has shown a remarkable effect on tumor pathology in preoperative high-stage gastric cancer patients

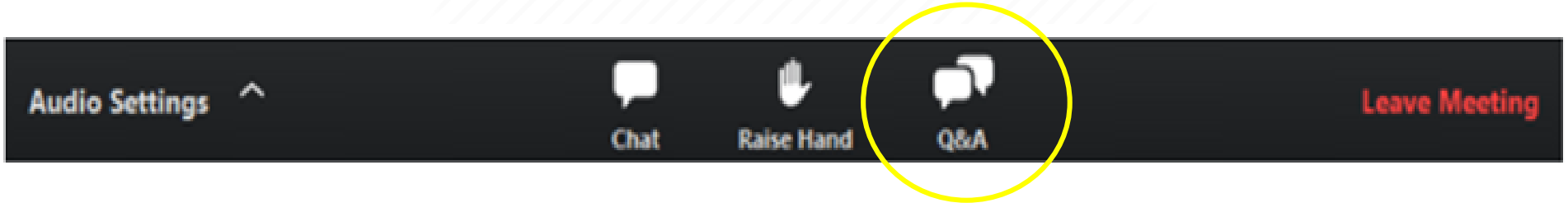
Recombinant Methinionase

- ***Recombinant methioninase (rMETase)*** was cloned from *Pseudomonas putida* (chemical name: l-methionine α-deamino-γ-mercaptomethane lyase)
- ***rMETase*** - tested in mouse models of human pancreatic cancer and macaque monkeys and a pilot Phase I trial of human cancer patients
- ***rMETase*** can also be given orally.
- ***Sequential combination therapy*** - Most promising application of rMETase therapy - Cancer cells within a tumor are trapped in S/G_2 by methioninase treatment and then treated with chemotherapeutic agents active against cells in S/G_2

Future of Cancer Research

Source: Labiotech

Post Your Queries!



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