Peptomyec: Treating cancer with anti-MYC mini proteins

Laura Soucek
Co-founder and CEO

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Cancer incidence in the world exceeds 14 million cases/year and causes >9 million deaths annually (CRUK)

**Current therapies:**
- Radio- and Chemotherapy
- Personalized medicine
- Immuno-therapy

**Challenges:**
- Resistance, lack of efficacy, toxicity

Peptomyc: Treating cancer with anti-Myc mini-proteins
Myc is a transcription factor deregulated in the majority of human cancers and essential for tumors to thrive (but not survival of normal cells).

...but no Myc inhibitor has reached the clinic yet.
The Myc/Max/Mad family of transcription factors controls cell proliferation, transformation, apoptosis and differentiation

- Myc belongs to the network of transcription factors Myc/Max/Mad.
- Members of this family form homo- or heterodimers to bind DNA via their B-HLH-LZ domain.
- Neither Myc nor Mad proteins can form homodimers: they must heterodimerize with Max to bind DNA and recruit other cofactors to regulate the transcription of their target genes.
- In contrast to Myc, the Max protein can form homodimers, and these are capable of binding to DNA but not to recruit co-regulators of transcription.
- The Max homodimers and Myc/Max heterodimers compete for a common DNA target site (the E-box). Rearrangement among these dimers provides a complex system of transcriptional regulation.

Peptomyc: Treating cancer with anti-Myc mini-proteins
Omomyc is a Myc inhibitor based on a truncated form of the c-Myc protein bearing mutations in the LZ.

- Myc/Max/Mad proteins share a B-HLH-LZ domain that enables them to form dimers and bind DNA.
- Omomyc consists of the B-HLH-LZ domain of c-Myc bearing 4 amino acid mutations in the LZ. Omomyc was designed by Dr. Soucek and published for the first time in 1998.
- The product of the Omomyc transgene is a 91 aa mini-protein.
- Omomyc is the best direct Myc inhibitor known to date (Whitfield et al., 2017).
Omomyc interferes with Myc binding to Max and to its targets on the DNA

**SCIENTIFIC BACKGROUND: MODE OF ACTION**

- Omomyc's mutations alter its dimerization specificity compared to Myc and enable Omomyc to displace the oncogenic Myc/Max heterodimers from their DNA binding sites and act as a potent Myc dominant negative.

- As a consequence, Omomyc induces cell cycle arrest and death of tumor cells.
The US experience (2001-2011)
1. SCIENTIFIC BACKGROUND: PROOF OF CONCEPT IN MICE WITH TRANSGENIC OMOMYC

Omomyc showed efficacy in various mouse models of cancer without severe side effects

- Lung cancer: Soucek et al., Nature 2008; Soucek et al., Genes & Dev 2013
- Skin cancer: Soucek et al., Cell death and diff 2004
- Pancreatic cancer: Sodir et al., Genes & Dev 2011
- Glioblastoma: Annibali et al., Nat Comm 2014

Kras^{G12D}

Kras^{G12D} + Omomyc
Back to Europe (2011)
1. SCIENTIFIC BACKGROUND: PROOF OF CONCEPT IN HUMAN TUMORS

Omomyc showed efficacy in the first patient-derived tumor samples
1. SCIENTIFIC BACKGROUND: THE MAJOR OBSTACLE

Can Omomyc itself be a drug?

The biggest challenge: It is a molecule too big and bulky to be directly delivered to cells.

“Omomyc is essentially just a proof of concept and can only work as gene therapy.”
Our pharmacological tool: Omomyc-derived peptides

(Beaulieu et al., Sci Transl Med 2019)
Intervention studies on tumor bearing mice

Beaulieu et al., 2019
The Omomyc mini-protein displays tropism for tumors and prevents their growth.
The Omomyc mini-protein reduces tumor growth and tumor grade (2.37 mg/Kg)
Efficacy of intravenous Omomyc in EGFR- P53- PI3K-mutated NSCLC subQ xenograft mouse model (H1975 human cell line, resistant to erlotinib)

H1975 cells were implanted subcutaneously into immunocompromised mice (growth was monitored with caliper measurements). Treatment started when tumors had reached 150 mm³. Mice were treated intravenously with 30mg/kg of Omomyc or vehicle injected intravenously once per week. In vivo (left) and ex vivo (right, at endpoint) measurements of tumor volume are shown (RTV = Relative).

Note: Omomyc displays a half-life of ~49 hours after i.v. administration
Unleashing the full potential of Omomyc: potential indications

3. CLINICAL PLAN – INDICATIONS

- Lung cancer
- Breast cancer
- Prostate cancer
- Colorectal cancer
- Ovarian cancer
- Hematologic malignancies (ALL, CLL, CML, MM, HL, NHL)

Peptomy: Treating cancer with anti-Myc mini-proteins
The company has funding to complete Phase Ia clinical trials

Next round of investment foreseen in 2020: 20 M euros to fund Phase IIa clinical trials
4. DEVELOPMENT PLAN AND TIMELINES

Fundraising highlights

**PUBLIC FUNDING:**
- SME instrument Phase I (European Commission): 50 K €
- PAT ACCIÓ (Generalitat): 50 K €
- RETOS Collaboración: 1.4 M € (between Peptomyc and lab)
- NEOTEC (CDTI): 210 K €
- APC (CDTI): 15K €
- ENISA: 300 K € (Loan)
- SME Phase 2 (H2020 Program): 2.2 M
- RETOS Collaboración: 2.1 M € (between Peptomyc and lab)

**PRIVATE FUNDING:**
- Seed Round in 2016 with VCs and BAs for 1 M euros
- Closed a series B of 4.2 M euros in 2017
- One more round series B’ of 5.7 M euros in 2020 (con el programa Innvierte)
5. TEAM

Peptomyc’s team: Strong science, Business acumen & Pharma out-licensing experience

**Board of Directors**

- Laura Soucek: Co-founder & CEO, Chair of the BoD
- M.-Eve Beaulieu: Co-founder & CSO
- Alexandra Maratchi: Business angel, CEO of Homuork
- Albert Ferrer: Director at Healthequity
- Montse Vendrell: Partner of Alta LS

**SAB of KOLs**

- Dr. Josep Tabernero: Director or VHIO, President of ESMO
- Dr. Enriqueta Felip: Head of Thoracic cancer unit at HUVH
- Dr. Aleix Prat: Head of Med Onco at Hospital Clinic
- Dr. Roger Stupp: Chief Neuro-onco, Northwestern Univ. (US), President EORTC

**Clinical and scientific team**

- Dr. Manuela Niewel: CMO
- Jörg Klumbis: CFO

**Partners & consultants**

- IP
- Legal
- CMC partners
- Non-clinical safety
- Regulatory
- Dechert
- Vetter
Peptomyc in the news

- **TV:**

- **Newspapers:**
  - [https://www.elmundo.es/ciencia-y-salud/salud/2019/03/20/5c923f25dddff904e8b45b3.html](https://www.elmundo.es/ciencia-y-salud/salud/2019/03/20/5c923f25dddff904e8b45b3.html)
  - [https://newsbeezer.com/mexicoeng/developed-a-drug-that-could-be-effective-against-most-tumors-news-from-gipuzkoa/](https://newsbeezer.com/mexicoeng/developed-a-drug-that-could-be-effective-against-most-tumors-news-from-gipuzkoa/)

- **Radio:**

- **Other:**
Summary: The Omomyc mini-protein penetrates cells and attacks MYC, resulting in safe and durable response in lung and breast tumors.

- Cell penetrating properties
- Preclinical efficacy in vivo (i.v. and local)
- Regulatory safety almost completed
- Industrial CMC
- To be licensed out @ CT Phase I (2022) or IIa (2024)
- Could treat several cancer types
- Patent portfolio (4 patents)
Disclosures Regarding Forward-Looking Statements
Peptomyc is including the following cautionary statement in this document to make applicable and take advantage of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 (or equivalent law) for any forward-looking statements made by, or on behalf of, the Company. Forward-looking statements include statements concerning plans, objectives, goals, projections, strategies, future events or performance, and underlying assumptions and other statements which are other than statements of historical facts. Certain statements contained herein, including, without limitation, those that are identified by the use of the words "anticipates," "estimates," "expects," "forecasts," "intends," "plans," "predicts," "projects," "believes," "seeks," "will," "may" and similar expressions, are "forward-looking statements". Forward-looking statements involve risks and uncertainties, which could cause actual results or outcomes to differ materially from those expressed in the forward-looking statements.
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