WORLD FEDERATION OF SCIENTISTS

International Seminars on Planetary Emergencies

57th Session

Erice, 7-13 August 2025

Medicine and Biotechnology PMP Session

Biomedical discoveries, preventive/therapeutic strategies and their risks

Franco M. Buonaguro

Chair of Medicine and Biotechnology PMP

Director Emeritus, UOC Molecular Biology & Viral Oncology

Ist. Naz. Tumori "Fond Pascale"

Napoli, Italy

Istituto Nazionale Tumori
Fondazione G. Pascale

2025 Topics of the *Medicine and Biotechnology* PMP Meeting

- Updates on current Infectious Diseases
  The Furine role in diseases:
  - Franco Buonaguro *The role of Furine in DNA virus infection and Cancers*
  - Massimo Ciccozzi *The FCS evolution in Coronaviruses*
  - Siguna Mueller *The biorisk of manipulating FCS: natural vs laboratory-driven viral evolution*
  - Per Hammarström: *The Brave New World of Biologic drugs - Safe and Effective?*

  Monitoring and controlling infectious disease outbreaks:
  - Ishwar Gilada *Alternative strategies to prevent/cure global virus-induced diseases*;
  - Sam Mbulaiteye *The EBV role in human diseases and current vaccine efforts*
- Updates on Neurodevelopmental Disorders and Neurodegenerative Disease
  The role of protein misfolding in Neurological (neurodegenerative and neuropsychiatric) diseases
  - Sofie Nyström *Amyloidogenic peptides*
  - Emanuele Buratti *TPD-43 misfolding and SLA*
  - Felice Iasevoli *Protein misfolding in neurodevelopmental and neurodegenerative disorders*
- Updates on Biotechnologies
  - William Crispin *From physics to Biomedicine: development of time-of-flight positron emission tomography (TOF-PET)*
  - Genoveffa Franchini *Australian HTLV-1 subtype C variant associated with lung morbidity in macaques*
- Updates on a new syndrome due to not-inherited somatic mutations
  - Neal Young *Somatic Mutations in VEXA syndrome*

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Session of the Medicine and Biotechnology PMP

15:30 **Session 2**: **Biomedical discoveries, preventive/therapeutic strategies and their risks**

Session Chairman: Franco Maria Buonaguro, Chairman Medicine and Biotechnology PMP

15.30 Massimo Ciccozzi: The Spike and the FCS evolution in Coronaviruses.
15:45 Sofie Nyström: Amyloidogenic peptides.
15:55 Emanuele Buratti: TPD-43 misfolding and SLA.
16:05 Felice Iasevoli: Misfolding in neurodevelopmental and neurodegenerative disorders.
16:15 Neal S. Young: Somatic Mutations in Vexa syndrome.
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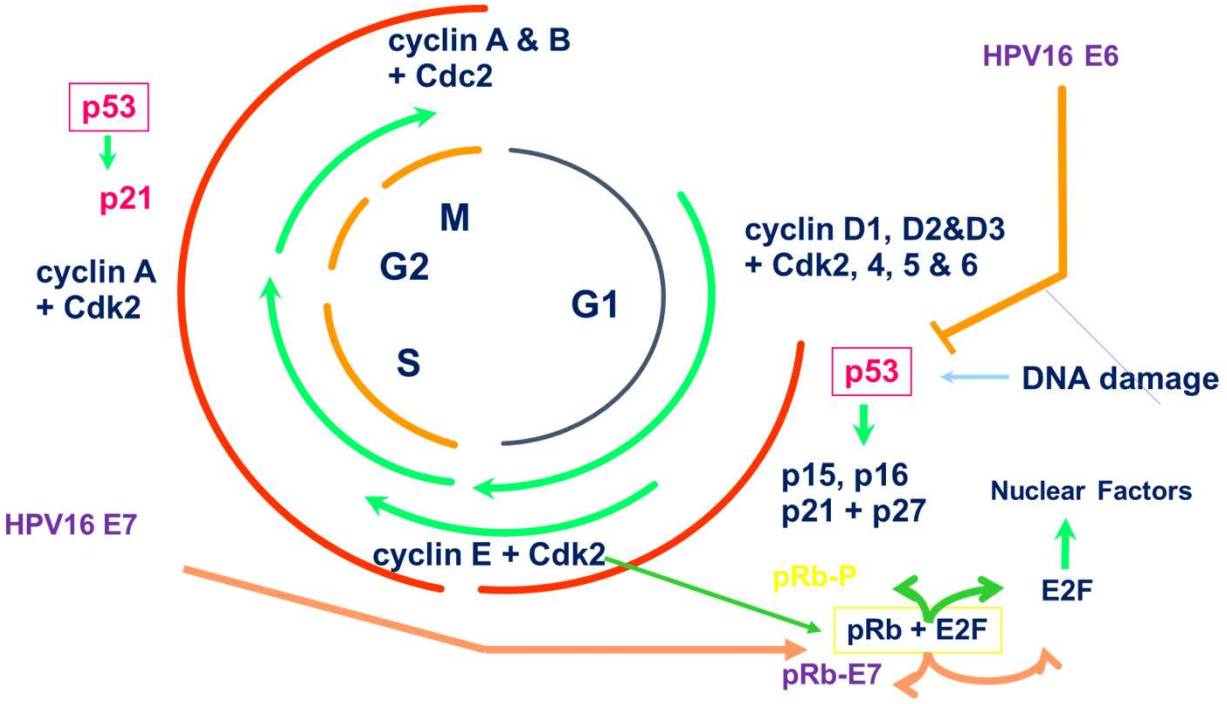
16:55 Per Hammarström: The brave new world of biologic drugs - safe and effective?
17:10 Discussion

HPV-driven cancers

Interactions between HPV-16 E6/E7 and Oncosuppressors



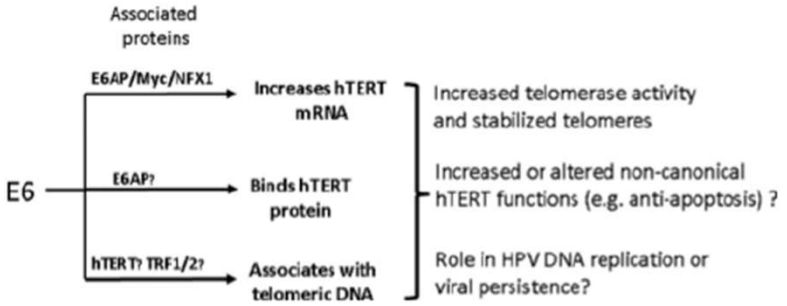
The E6 oncoprotein interacts with E6AP to reduce p53 and to increase hTERT activity

HPV E6 protein interacts physically and functionally with the cellular telomerase complex

Xuefeng Liu, Aleksandra Dakic, Yiyu Zhang, Yuhai Dai, Renxiang Chen, and Richard Schlegel[1]

Department of Pathology, Georgetown University Medical School, 3900 Reservoir Road, Washington, DC 20057

Edited by Peter M. Howley, Harvard Medical School, Boston, MA, and approved September 24, 2009 (received for review June 8, 2009)



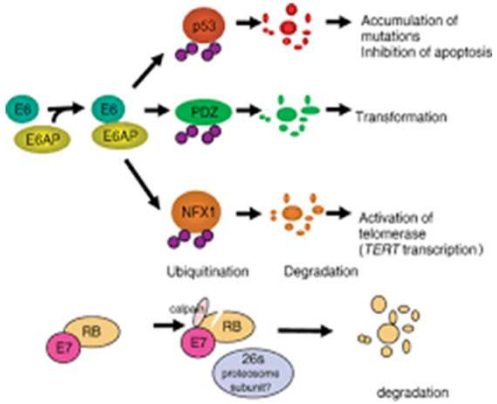
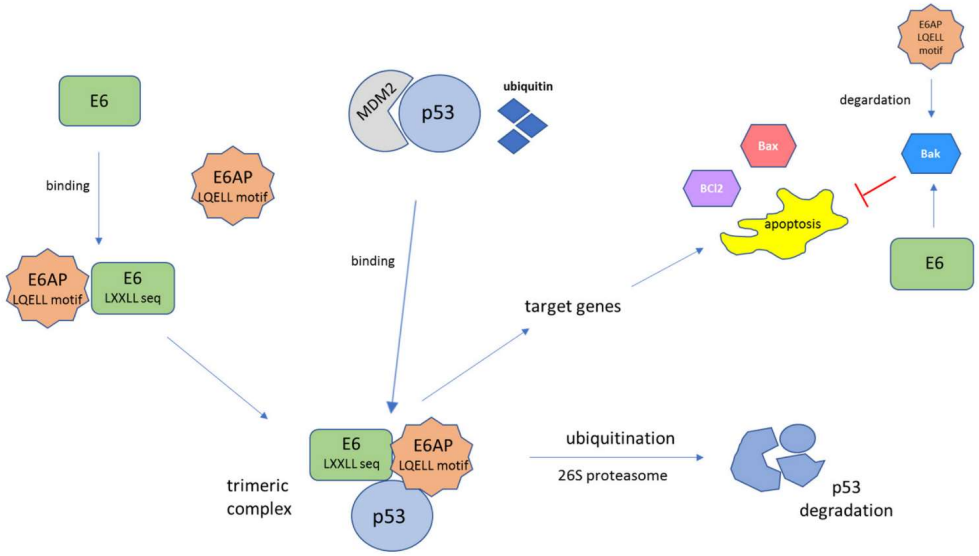


Fig. 7. E6 regulation of hTERT function and its possible roles in cell immortalization and HPV biology. Using information from this and previous studies (6, 13–16, 18, 21, 23, 55), we illustrate how HPV E6 can regulate telomerase, telomere function, and hTERT function at multiple levels. The top line summarizes the ability of E6 to transactivate the hTERT promoter via interactions with E6AP/Myc/NFX1–91 and stabilize hTERT mRNA through interactions with NFX1–123. The second and third lines summarize the findings of the current study where E6 has been shown to bind directly to hTERT as well as to telomeric DNA. Hypothetical consequences of these interactions are indicated, including possible alterations in the noncanonical functions of hTERT.

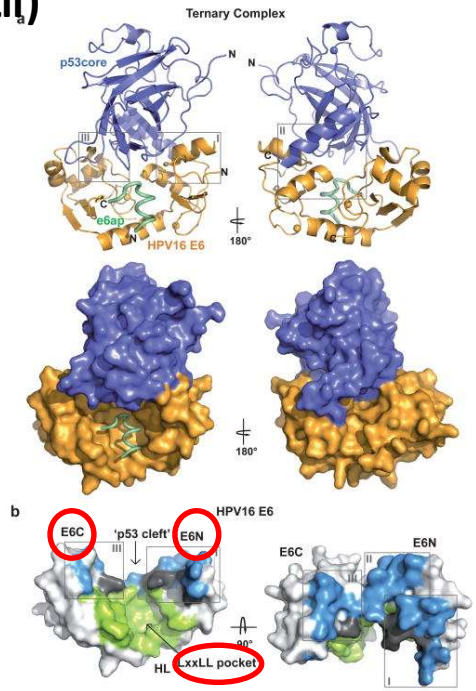
www.pnas.org/cgi/doi/10.1073/pnas.0906357106

The p53 ubiquitination

E6/E6AP/p53 complex (LXXLL motif)



Haręża DA, et al. Int J Mol Sci. 2022



Martinez-Zapien D, et al., *Nature*. 2016

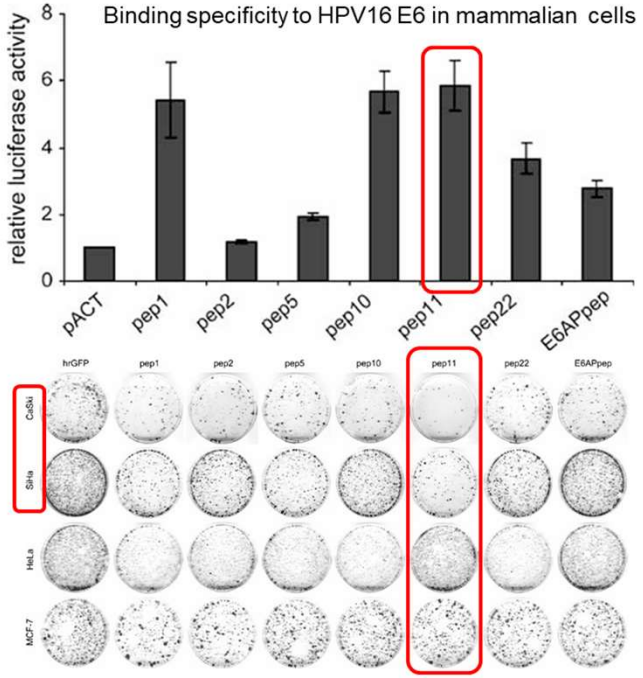
Anna Lucia Tornesello

Development of peptides binding HPV16 E6 oncoprotein

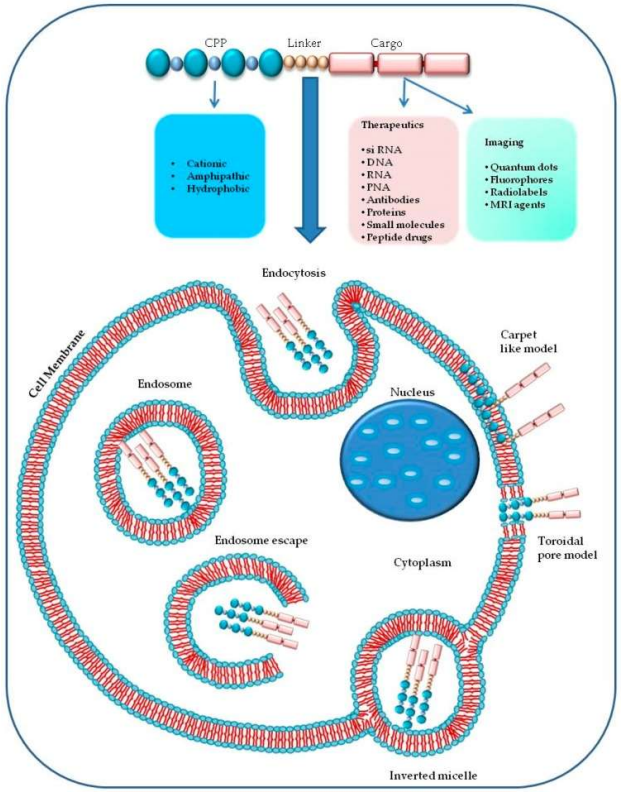
Library of peptides bound by HPV16 E6

pep1	KGSLN**CSCLVCWLQMFLGE**FGP
pep2	GWECVLWSDFEWPCACWGLHGP
pep5	PFLLG**CFCLCCWIECQIG**SYGP
pep10	SGGGDSFSWAMAFYF**LDTLLG**P
pep11	EFGSG**CSCIVCI**GLI
pep22	GMFTGESWVSSSLMV**LDALLG**P
novel motif	**CXChXCh**
E6AP motif	**LbXhLsa**

An expression library of randomised linear 20-mer peptides linked to the transcriptional activation domain of GAL4 was created and screened for HPV16 E6 binding properties by yeast two-hybrid assaY. Six peptides were selected among which a new binding motif was found.



Dymalla S, et al., J Mol Med (Berl). 2009



Borrelli A, Tornesello AL., et al. Molecules. 2018.

Cell Penetrating Peptides: Biot-CPP-PEP11 inhibiting E6-mediated p53 degradation

AIM

CPP - pep11

Biot-RRRRRR-EFGSGCSCIVCIGLI-NH_2

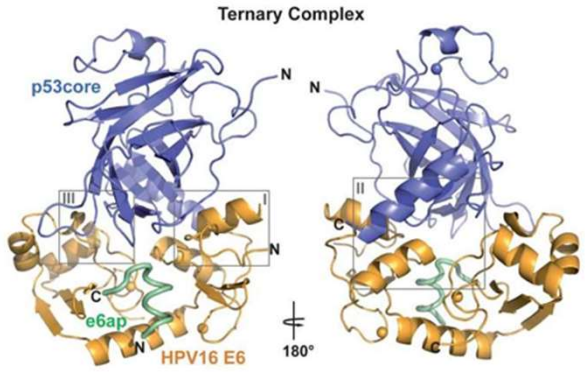
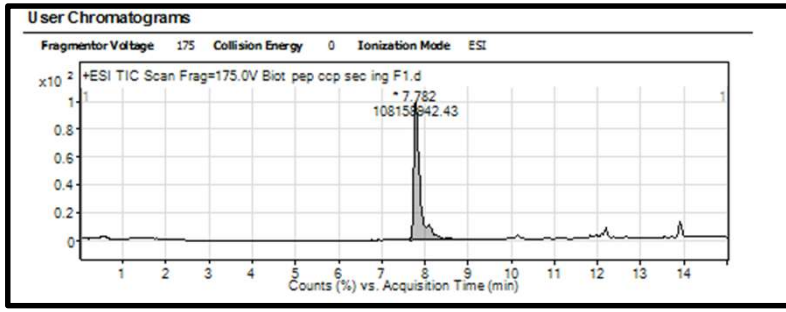


Figure 1: Structure of the HPV16 E6/e6ap/p53core ternary complex (green: E6AP peptide, gold: HPV16 E6, purple: p53 core[3]. Biotin was bound to the N-terminus.

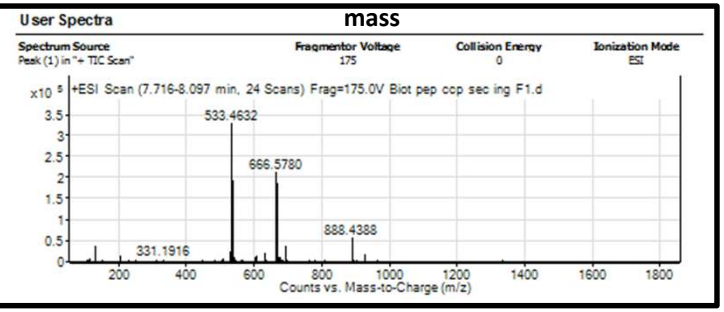
Modification of peptides binding HPV16 E6 oncoprotein

Pep11	EFGSGCSCIVCIGLI-NH_2
CPP-Pep11	RRRRRR-EFGSGCSCIVCIGLI-NH_2
Biot-CPP-Pep11	Biotin-RRRRRR-EFGSGCSCIVCIGLI-NH_2

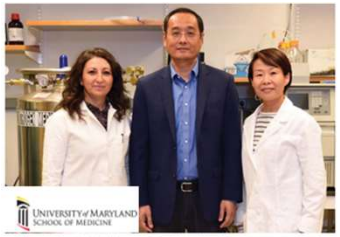
HPLC-MS showing high quality of peptide obtained by Boc chemistry



The MALDI technology displays the peptide's corresponding mass

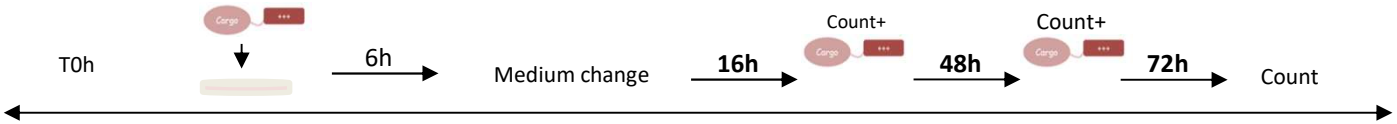


All the peptides used were synthesized in Baltimore at the Human Virology Institute, department of chemistry and biochemistry by using solid phase with Boc chemistry which is a methodology now replaced by Fmoc specifically for peptides. Importantly, they initially used Fmoc chemistry but the yield of the peptide was particularly low. Moreover, it is to undernote that it was not possible to synthesize the peptide sequence without the adding of CPP due to its high hydrophobic nature, that makes it practically impossible to solubilize for any applications.

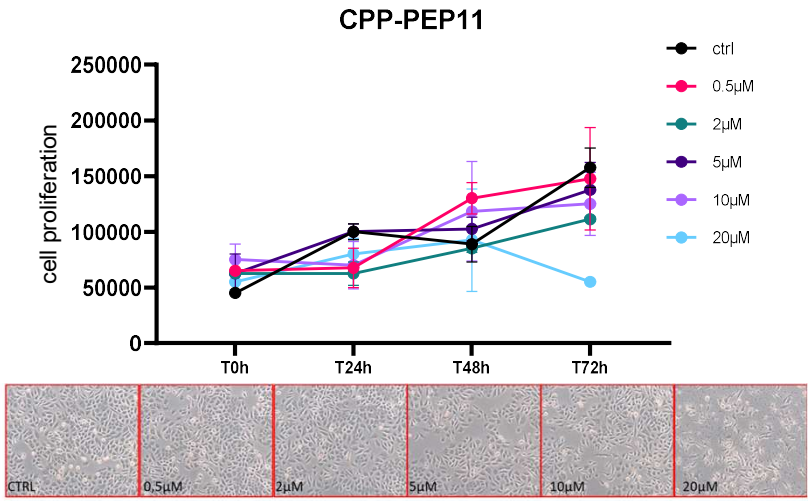


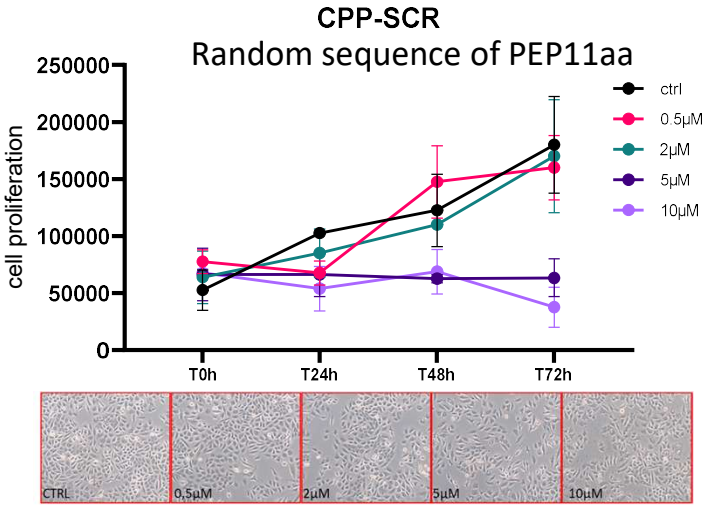
Anna Lucia Tornesello with Prof Wuyuan Lu, Fudan Univ

Dose-response analysis over a range of concentrations of CPP-PEP11

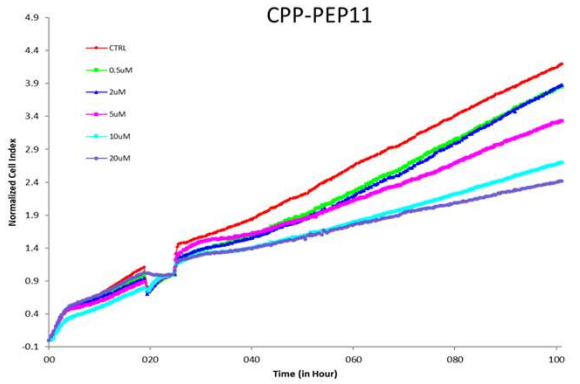


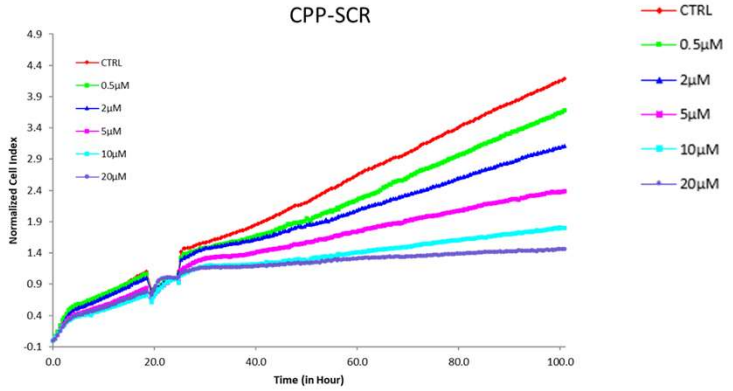
HPV16 positive cervical cancer **SiHa cell line** (p53 wild type) were used for these studies.

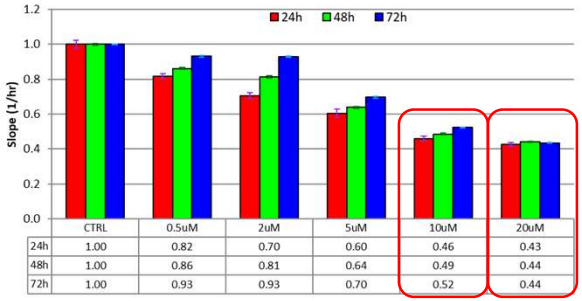




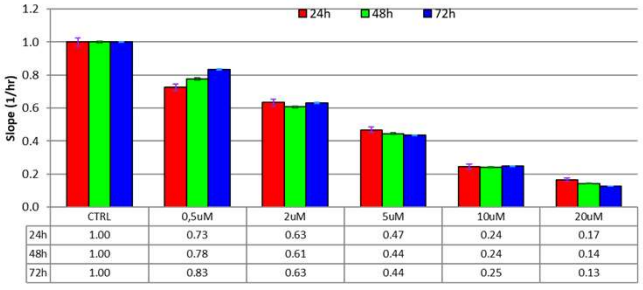
CPP-PEP11 reduces cell proliferation in a dose-dependent manner by XCELLigence technology







	CTRL	0.5uM	2uM	5uM	10uM	20uM
24h	1.00	0.82	0.70	0.60	0.46	0.43
48h	1.00	0.86	0.81	0.64	0.49	0.44
72h	1.00	0.93	0.93	0.70	0.52	0.44

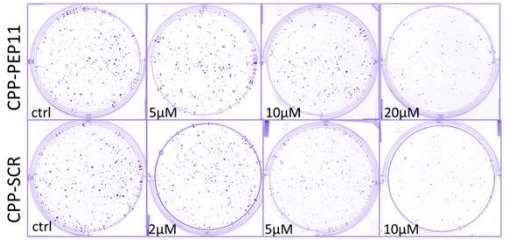


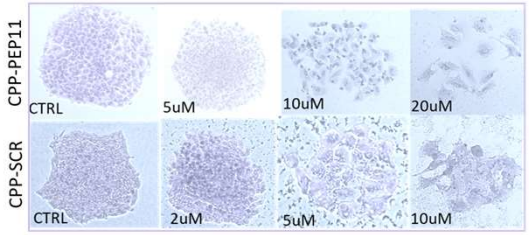
	CTRL	0,5uM	2uM	5uM	10uM	20uM
24h	1.00	0.73	0.63	0.47	0.24	0.17
48h	1.00	0.78	0.61	0.44	0.24	0.14
72h	1.00	0.83	0.63	0.44	0.25	0.13

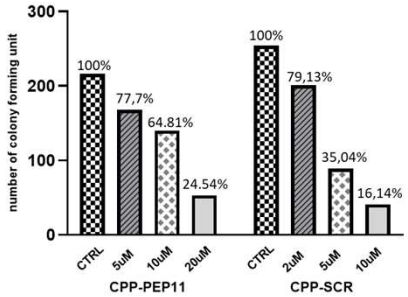
Luisa Dassi

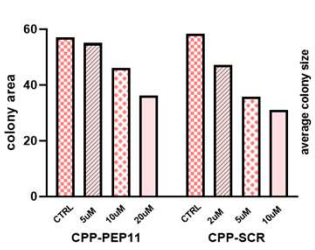
Effect of CPP-pep11 on cell survival:

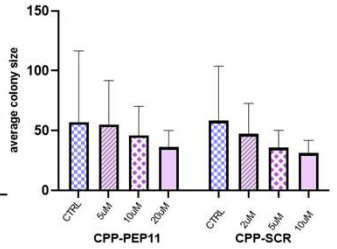
CPP-pep11 reduces the ability of SiHa to proliferate



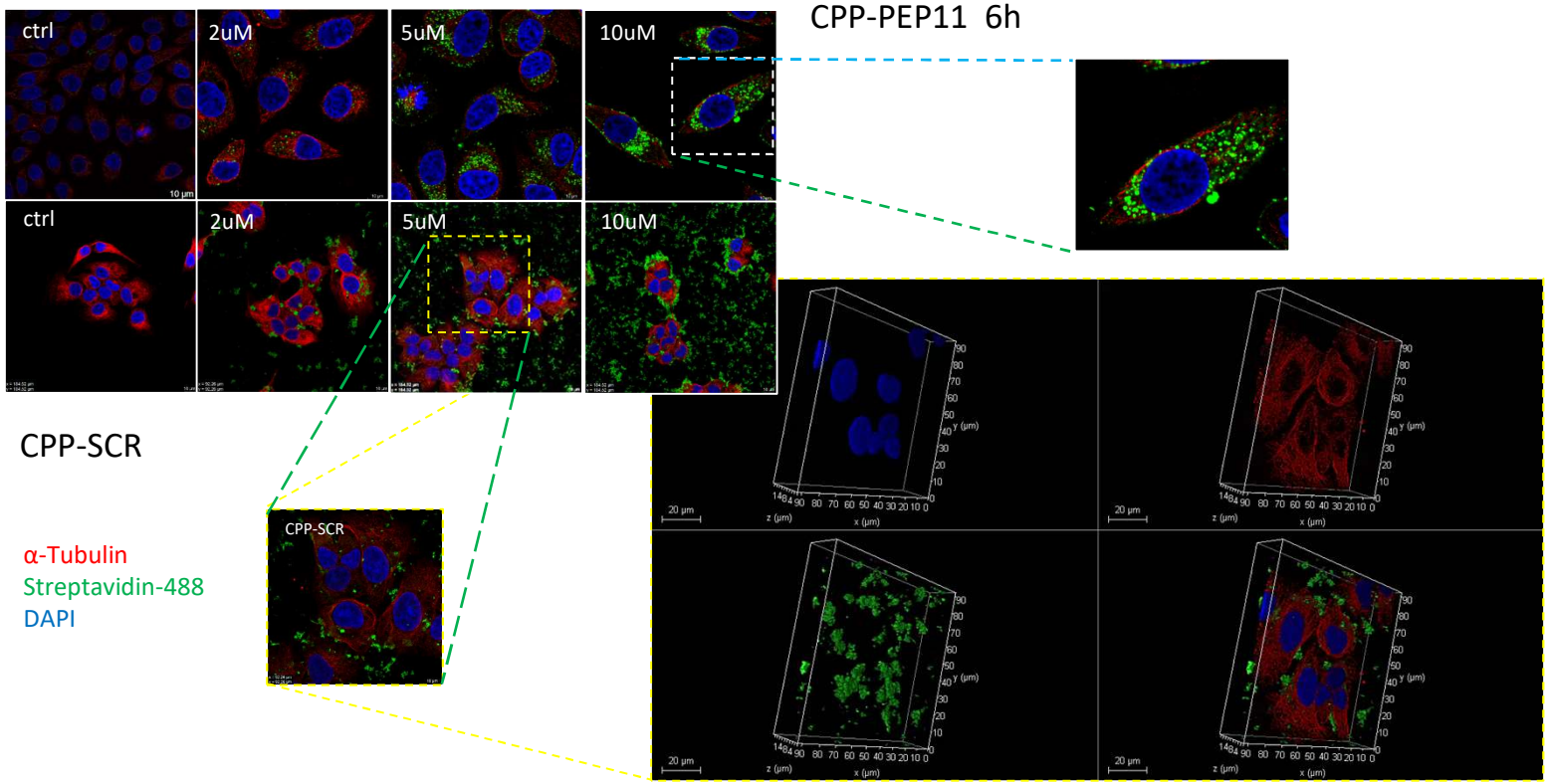




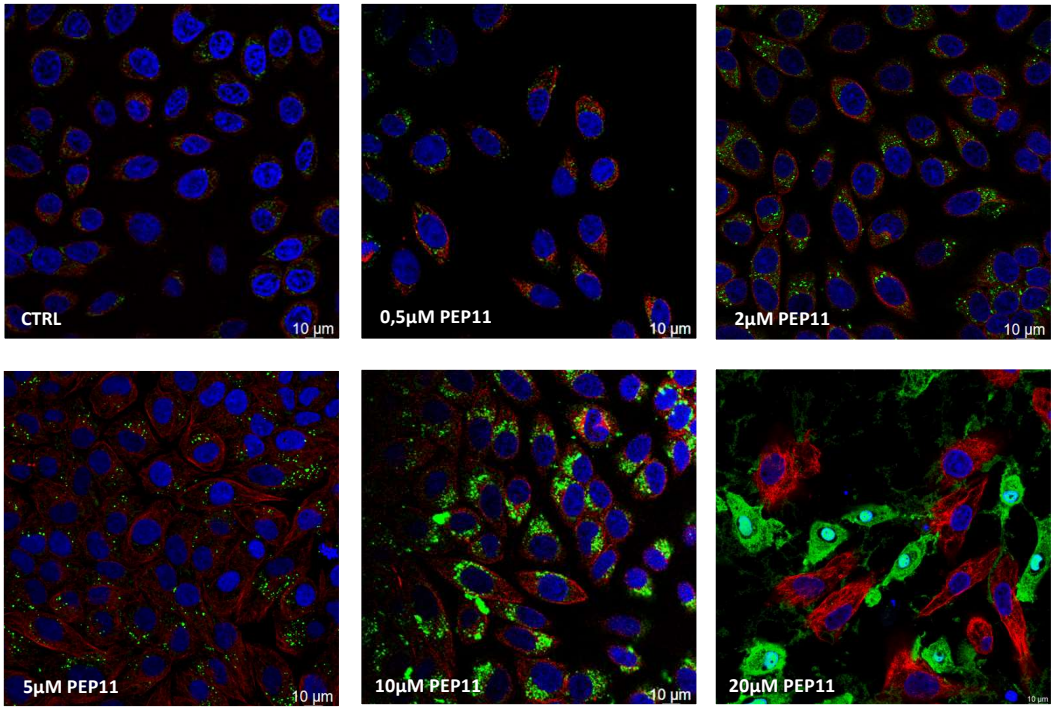




CPPs internalization

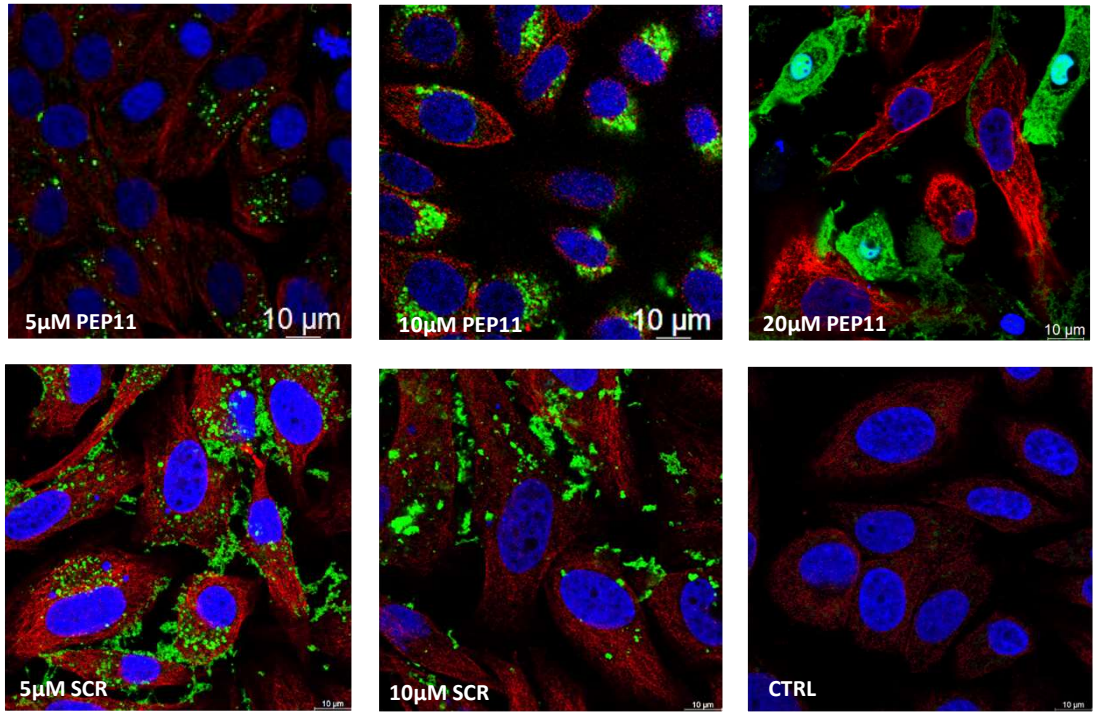


BIOT-CPP-PEP11 localization at 48h



DAP
STREP-488
α-
tub

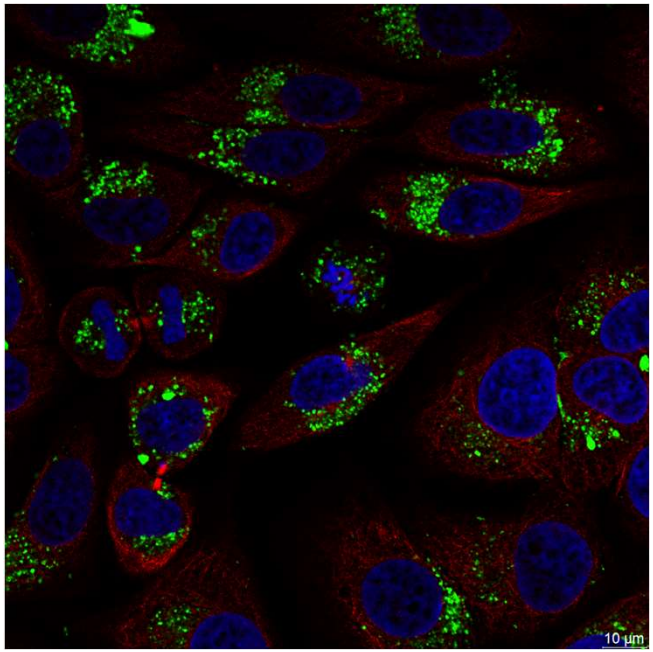
BIOT-CPP-PEP11 and Biot-CPP SCR localization



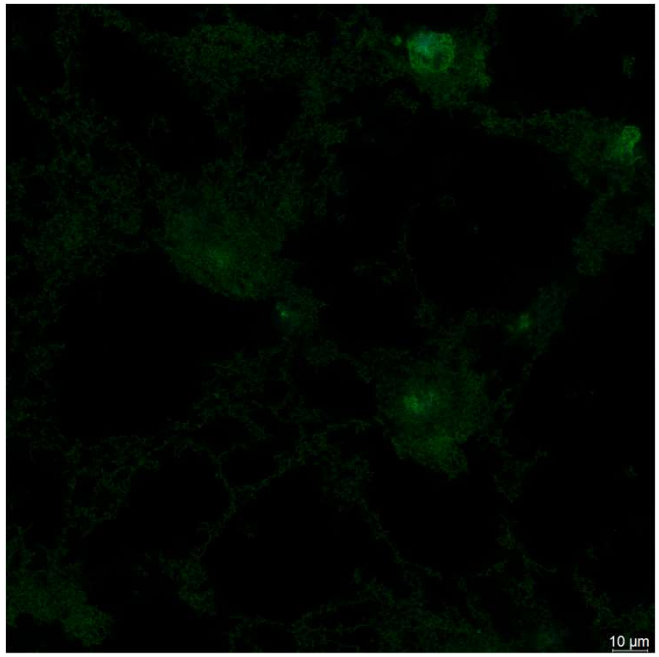
DAP
STREP-488
α-
tub

BIOT-CPP-PEP11 localization (4days)

- CPP-PEP11 10uM



- CPP-PEP11 20uM



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