THE POTENTIAL OF PLANTS AS RAPID-RESPONSE EXPRESSION PLATFORMS FOR PANDEMIC RESPONSE

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Molecular f

Unique advantages to producing prot

- Lower cost as biomass **much** cheape
- Less stringent / expensive infrastruc
- **Much more rapidly scalable** than ar
- Support eukaryotic PTMs & assemb

vs

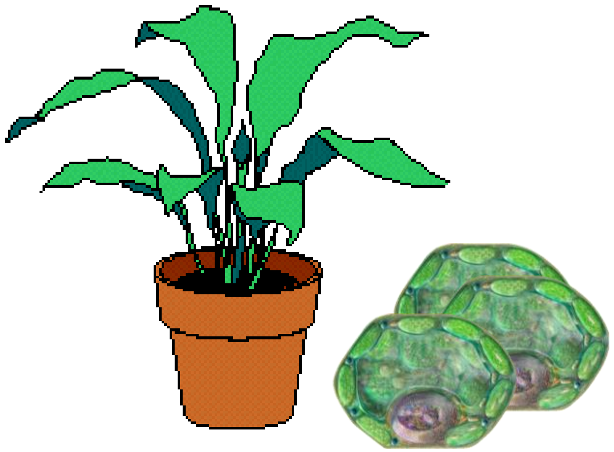
Expression of proteins in plants

Cost of biomass: 100 – 1000-fold < animal cell and 10 – 100-fold < bacterial or yeast cell production

DNA coding for protein

Introduce into plants or cells by transient transfection with *Agrobacterium*

OR transgenic

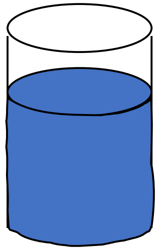


Cheap AND infinitely scalable

Expensive downstream processing

= conventional processes

Harvest, extract protein



Formulate for Injection OR oral dosing

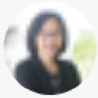
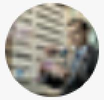
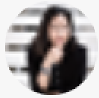
DOSE HUMANS

OR ANIMALS

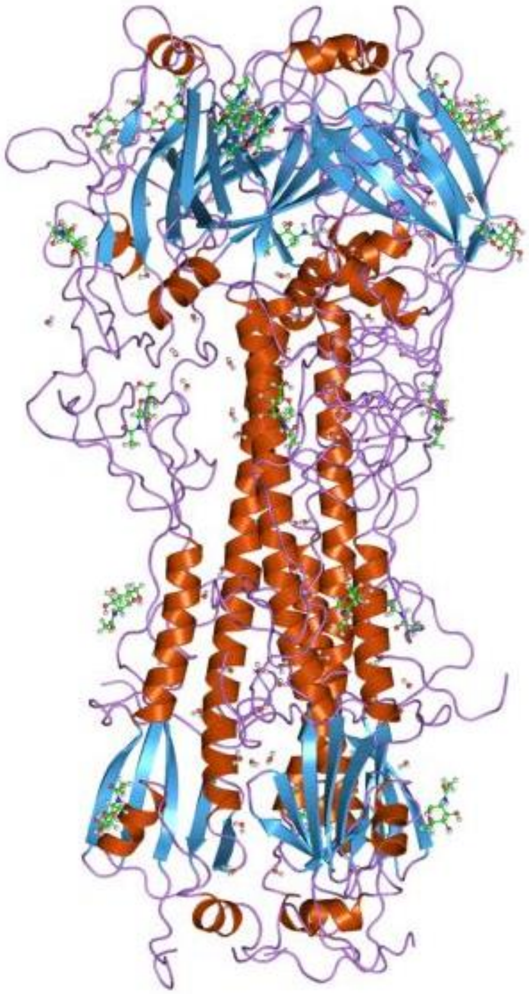
Front. Plant Sci., 28 September 2022
Sec. Plant Biotechnology
https://doi.org/10.3389/fpls.2022.901978

This article is part of the Research Topic
Plant Science's Contribution to Fighting Viral Pandemics: COVID-19 as a Case Study, Volume II
View all 4 Articles ›

A recombinant subunit vaccine candidate produced in plants elicits neutralizing antibodies against SARS-CoV-2 variants in macaques

Narach Khorattanakulchai[1,2], Kanjana Srisutthisamphan[3], Balamurugan Shanmugaraj[4], Suwimon Manopwisedjaroen[5], Kaewta Rattanapisit[4], Chalisa Panapitakkul[1,2], Taratorn Kemthong[6], Nutchanat Suttisan[6], Suchinda Malaivijitnond[6],  Arunee Thitithanyanont[5],  Anan Jongkaewwattana[3] and  Waranyoo Phoolcharoen[1,2*]

H5N1 Influenza HA Expression Results

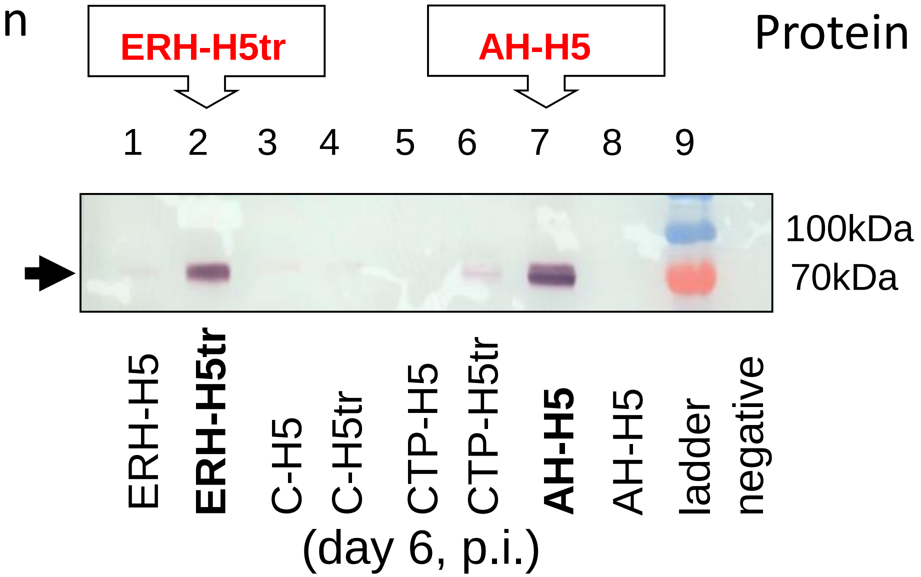


HA gene human codon optimised, full length (H5) and transmembrane domain truncated (H5Tr) versions made

Protein retained in ER by KDEL tag

Protein exported

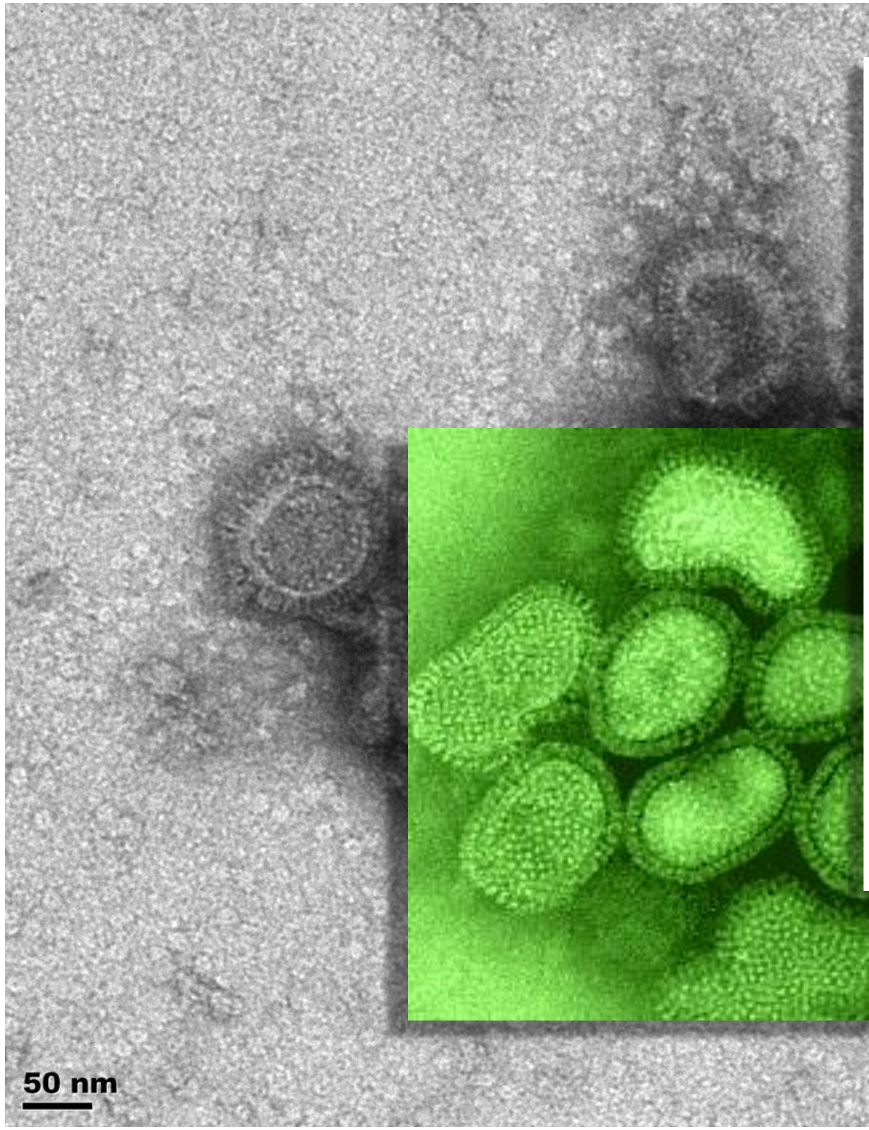
Transient



Transient = 0.8 g protein / kg plant material
Stable transgenics = 0.3 g protein / kg plant material

Mortimer et al. 2012 BMC Biotechnology 12:14

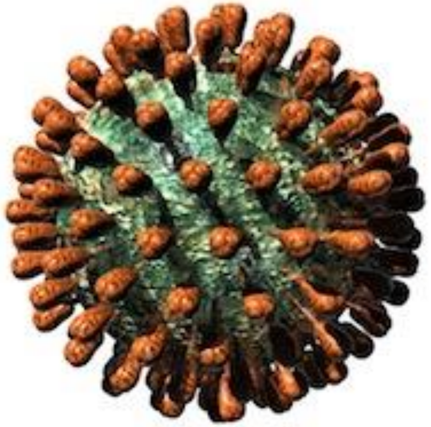
H5 HA Budding as VLPs in Plants



Greatly increased immunogenicity

Use as platform for display of other GPs or epitopes:

- **HIV Env***
- Ebola GP
- **Coronavirus S**
- Rabies G
- **Rift Valley fever virus Gn***
- **Influenzavirus A M2e***



2021: "…a plant-made 4-valent seasonal influenza vaccine is at least equivalent to conventional egg-made vaccine, and possibly better at eliciting cellular responses because of its nature as virus-like particles instead of subunit proteins.

There are no other viable VLP-based flu vaccines available. The clinical trial results established the vaccine candidate as a viable alternative to conventional offerings, and moreover, one that can be very quickly tailored to account for changes in circulating influenza virus strains, unlike egg production which involves a 6-month turnaround."

https://www.infectiousdiseaseadvisor.com/home/topics/respiratory/influenza/plant-based-vaccines-higher-cellular-response-for-influenza-potential-coronavirus/

Seasonal Flu

Medicago's team is developing a quadrivalent and adjuvanted virus–like particle (VLP) influenza vaccine candidate.

Disclaimer: This vaccine is not approved for use in humans.

Learn more about Influenza →

- First produced as cGMP batches in early 2020
- Licenced for use in Canada in February 2022 after Phase 3 trials

frontiers in Plant Science

ORIGINAL RESEARCH
published: 13 September 2021
doi: 10.3389/fpls.2021.738619

A Plant-Produced Virus-Like Particle Displaying Envelope Protein Domain III Elicits an Immune Response Against West Nile Virus in Mice

Jennifer Stander[1], Aleyo Chabeda[2], Edward P. Rybicki[1,3] and Ann E. Meyers[1*]

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SPYTAG / SPYCATCHER System

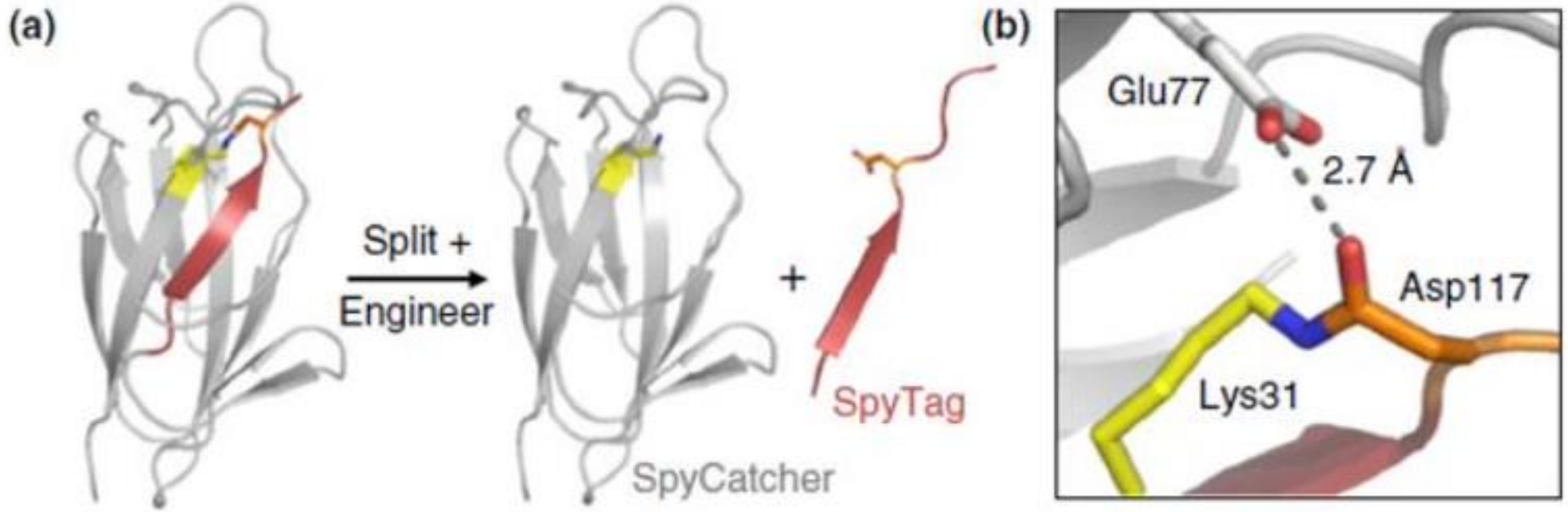
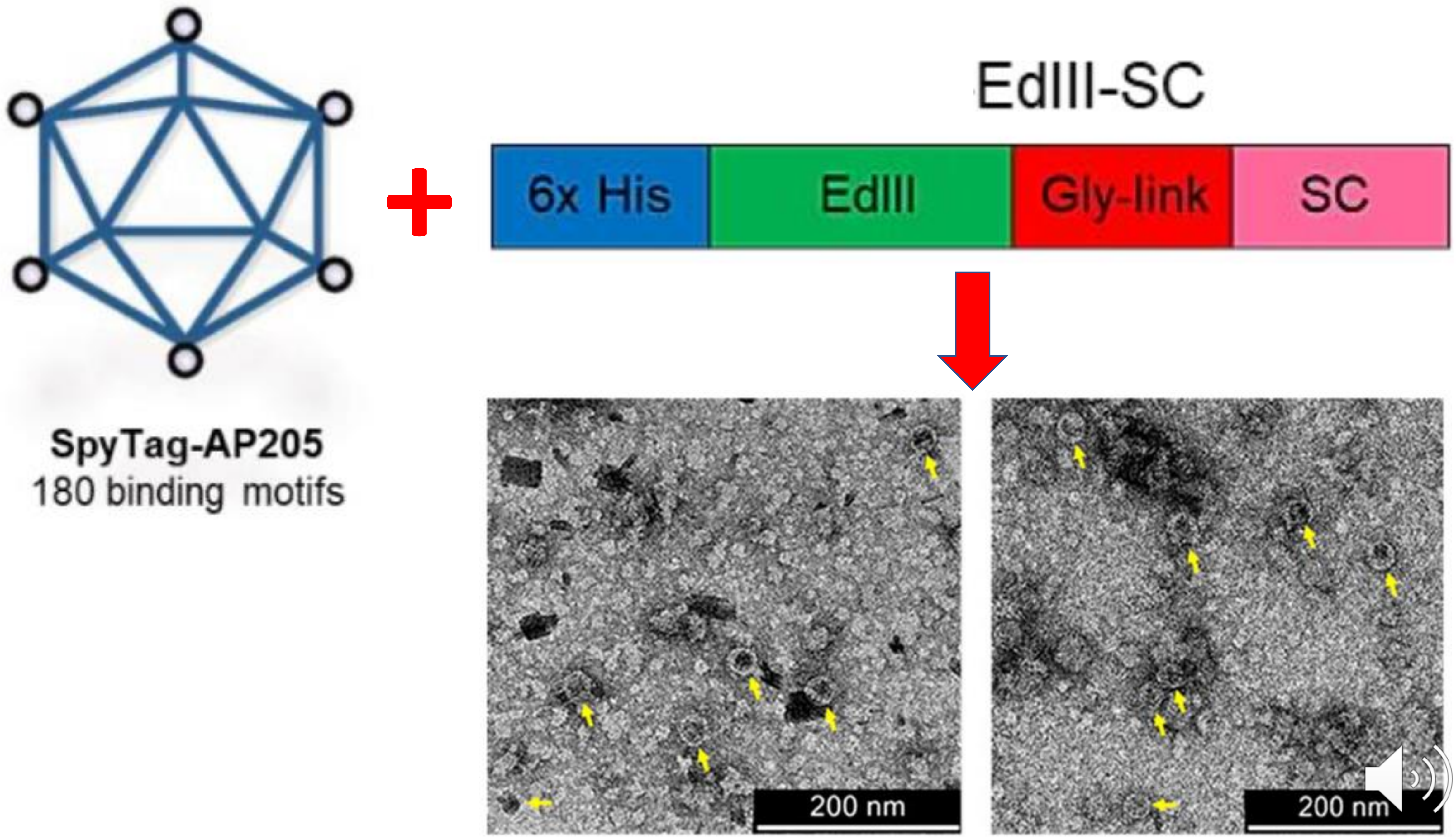
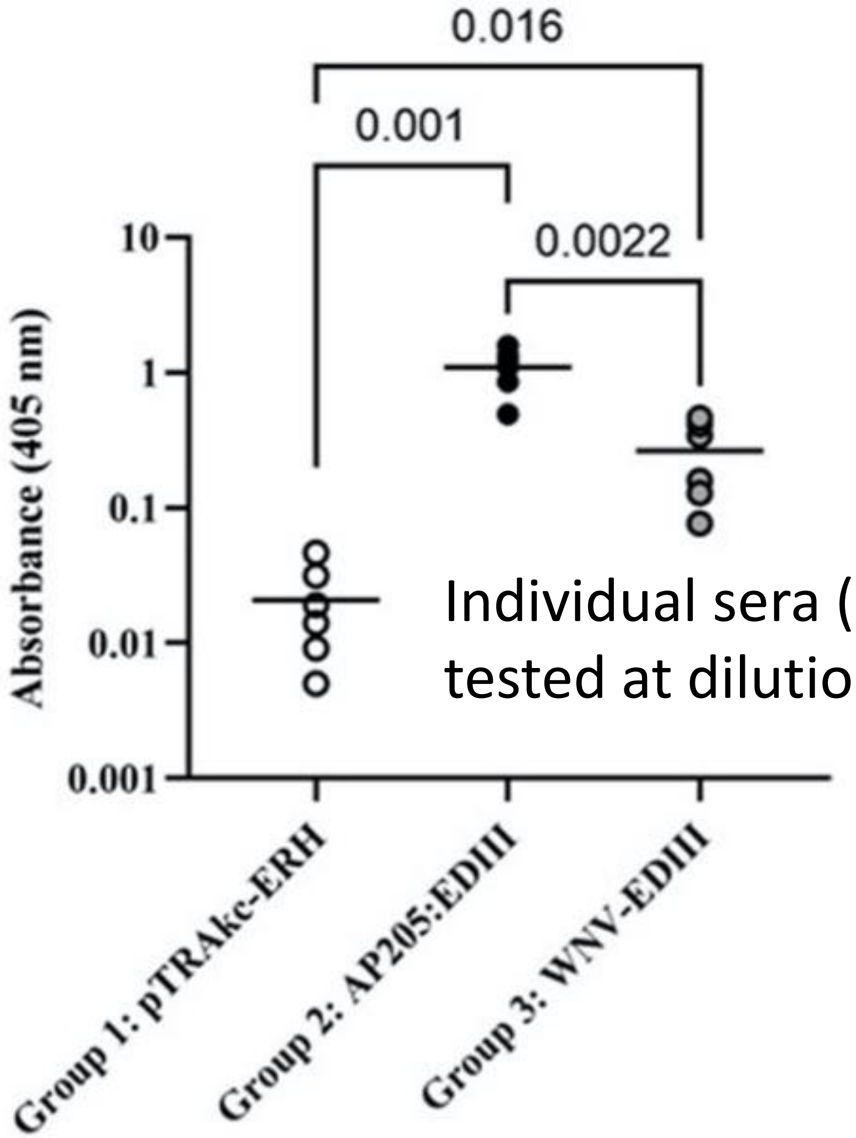


Figure 1.8. Generation of SpyTag/SpyCatcher. **(A)** Schematic of CnaB2 splitting into ST (red) and SC (grey). **(B)** The environment of the isopeptide bond between Asp117 (carbons orange) and Lys31 (carbons yellow), facilitated by Glu77 (carbons grey). Article open access. (Reddington & Howarth, 2015).

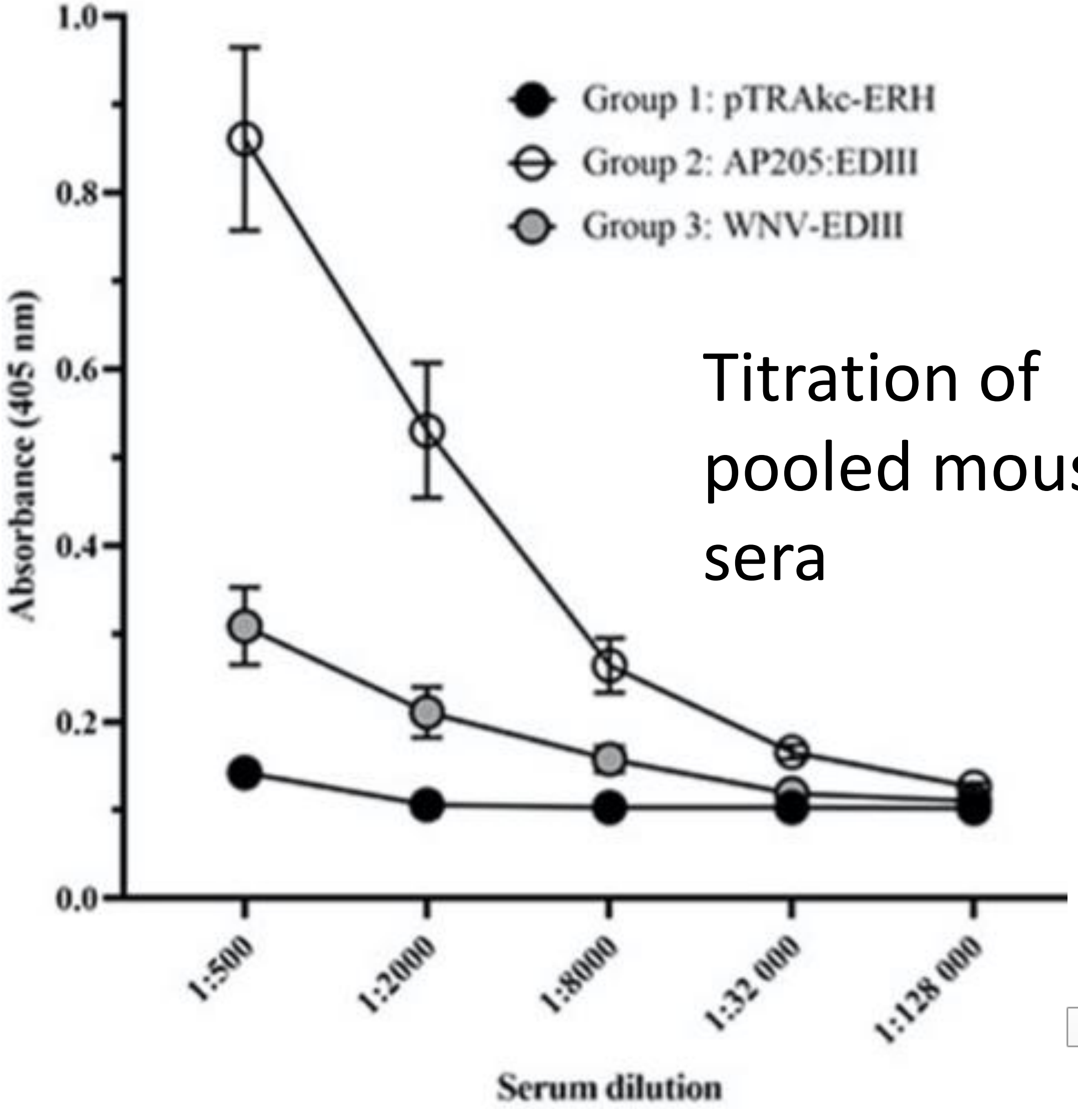

SpyTag-AP205
180 binding motifs
EdIII-SC
6x His
EdIII
Gly-link
SC
200 nm
200 nm

Mouse Immunogenicity

BALB/c mice were immunised with three doses of 5 µg each

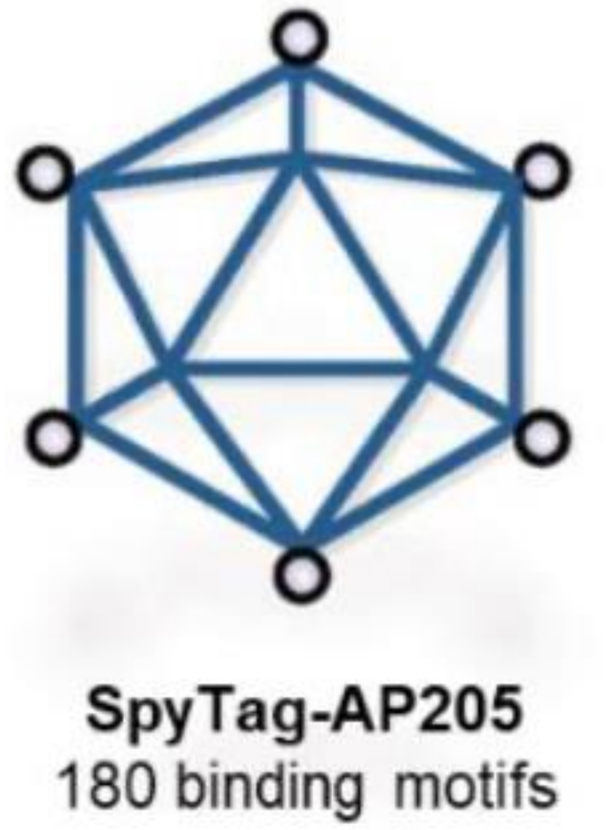


Individual sera (n = 6) tested at dilution of 1:1,000



Titration of pooled mouse sera

Pan-flavirus vaccine?



EDIII Domains + SpyCatcher

Yellow fever virus

Dengue viruses

Zika virus

West Nile virus

Japanese encephalitis virus

Tick-borne encephalitis virus

Manufacture at cGMP, stockpile

Manufacture at cGMP separately, stockpile

Future Applications - 1:

Rapid, local, inexpensive small-scale manufacture of lab / diagnostic reagents:

Rapid response reagents can also be quickly made in University labs or diagnostic facilities, as required, by sharing of cloned DNA and transient expression in plants. These include:

- Pathogen antigens
- Monoclonal Abs
- Detection reagents eg: anti-human::HRP conjugate
- RNA positive control for RT-PCR in plant virus coat

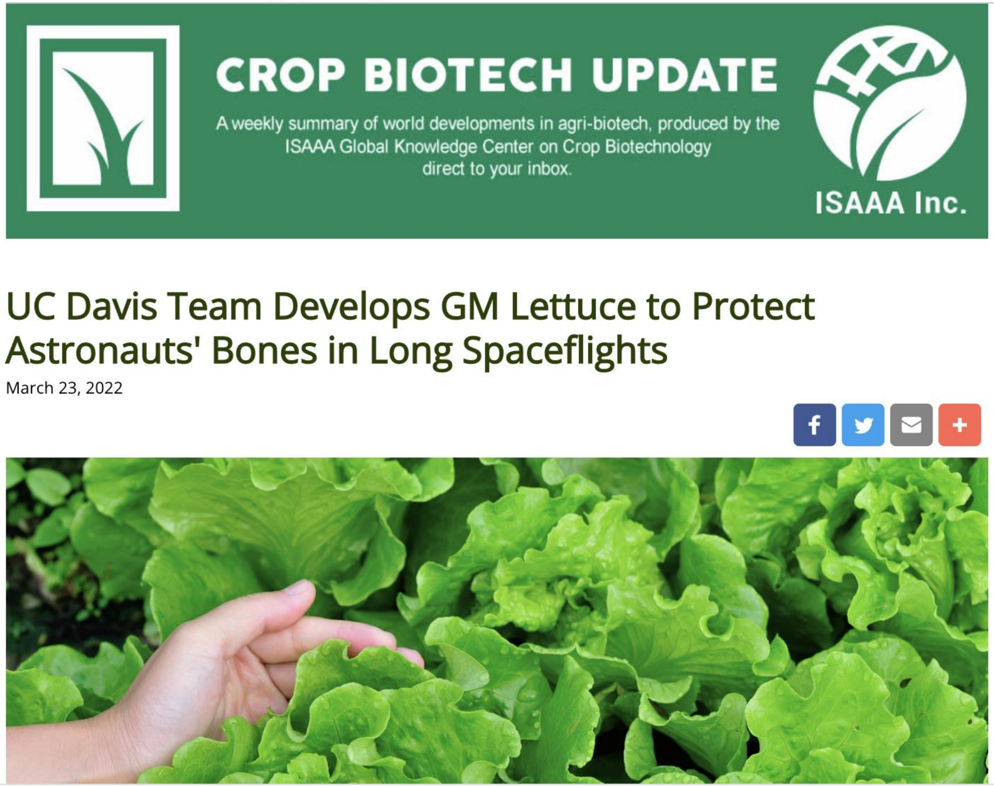
Future Applications - 2:

Localised large-scale manufacture of vaccines:

- Vaccines that are required to be cheap for extended EPI purposes and wide coverage – eg: influenza, SARS-CoV-2
- Rapid-response vaccines for "orphan" or neglected diseases (Lassa, Marburg, Ebola, Sudan, Nipah viruses) near points of outbreak – including RNA vaccines

LMICs manufacture of monoclonal antibodies, therapies

- Much cheaper antibodies for infectious and non-infectious disease therapy (HIV, RSV, rheumatoid arthritis, breast cancer, snake bite)
- Cheaper prophylactics & therapeutics for humans and animals – e.g. to combat antibiotic resistance in microbial populations



Conclusion

PMF could be the gateway technology that allows most countries to participate in all levels of the One Health Initiative: making reagents for use as diagnostics that could also be used as therapeutics or rapid-response vaccines for diseases of animals, and even humans