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VABILO NA PREDAVANJE
V OKVIRU DOKTORSKEGA ŠTUDIJA
KEMIJSKE ZNANOSTI

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z naslovom:

**Production of protein biotherapeutics in plants:
a long and winding road to victory**

**v sredo, 14. 4. 2021 ob 15. uri,
preko spletnega orodja Zoom**

[https://bokuvienna.zoom.us/j/99909593371?pwd=a01MbVh
MUUZxRzZhwMnRYNjlsVnF6dz09](https://bokuvienna.zoom.us/j/99909593371?pwd=a01MbVhMUUZxRzZhwMnRYNjlsVnF6dz09)

(Meeting-ID: 999 0959 3371, Kenncode: 121912)

Vljudno vabljeni!

Abstract:

The tobacco variant *Nicotiana benthamiana* has recently emerged as a versatile host for the manufacturing of protein biotherapeutics. Several studies have demonstrated that broadly neutralizing antibodies (bNAbs) to human immunodeficiency virus type 1 (HIV-1) can be effectively produced in *N. benthamiana*. However, the integrity of many anti-HIV-1 bNAbs generated in this expression platform is compromised by inadvertent proteolysis. In particular, cleavage events within the complementarity-determining-region (CDR) H3 loops of the heavy chains lead to strong reduction of the antigen-binding potencies of proteolysis-sensitive antibodies. Inhibitor profiling experiments revealed that bNAb fragmentation in *N. benthamiana* is largely due to the action of serine proteases belonging to the subtilisin superfamily. We have now identified two subtilisin-like serine proteases (NbSBT1 and NbSBT2) whose combined action is sufficient to account for all major cleavage events observed upon expression of different bNAbs in *N. benthamiana*. Hence, down-regulation of NbSBT1 and NbSBT2 activities could constitute a powerful means to optimize the performance of this powerful platform for the production of biopharmaceuticals.

Human angiotensin-converting enzyme 2 (ACE2) is the primary host cell receptor for Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). Soluble ACE2 can be utilized as a potent decoy receptor to block the interaction of SARS-CoV-2 with target cells and thus offers great promise for the treatment or prevention of coronavirus disease 2019 (COVID-19). We have now generated a recombinant soluble ACE2 variant in *Nicotiana benthamiana* and compared its enzymatic, ligand-binding and virus-neutralizing activities with those of soluble ACE2 made in mammalian cells. Our data reveal that plant-derived ACE2 is fully functional with regard to enzyme activity, affinity to the SARS-CoV-2 receptor-binding domain and SARS-CoV-2 neutralization, thus demonstrating that *N. benthamiana* is a suitable host for the rapid and efficient production of protein biotherapeutics targeted at COVID-19.