Agonists of Bacterial ClpP as potential antibacterial agents. Project CASABI (MICINN)

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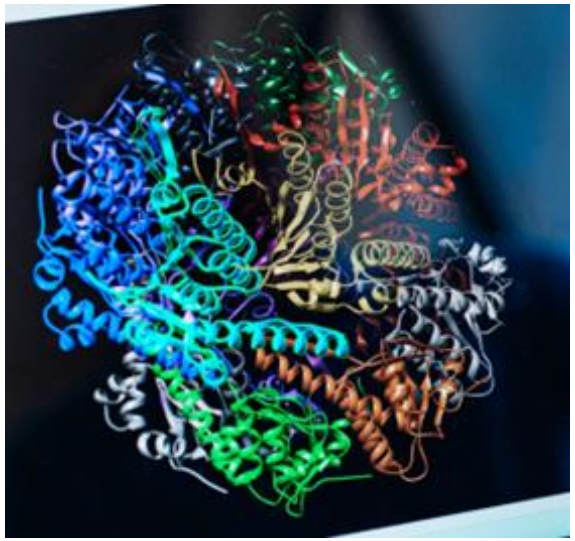
Ref # PLEC2022-009507



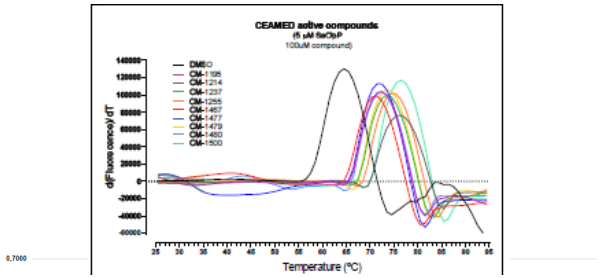
It has been reported that activation of ClpP in bacteria can reduce the infectivity and virulence of both Gram-positive and Gram-negative bacteria.
Furthermore, agonists of bacterial ClpP can reduce the growth of multidrug resistant bacteria and can act synergistically with several approved antibiotics.

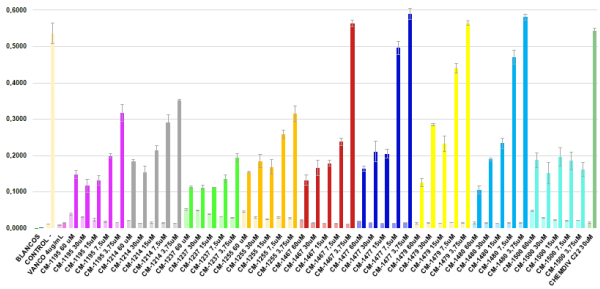
The objective of this project is to develop new families of antimicrobial compounds based on the selective activation of ClpP, and investigate their *in vivo* effects on bacterial infections.

Target ClpP: S *aureus* (SaClpP)

This project has recently identified modification to some small molecular activators of HsClpP, that renders them more selective for SaClpP.

Potencies in drug resistant forms of *S Aureus* and E. *faecalis* are better than several currently used antibacterial agents.





CEAMED

Agonists of ClpP to treat resistant cancers and bacteria

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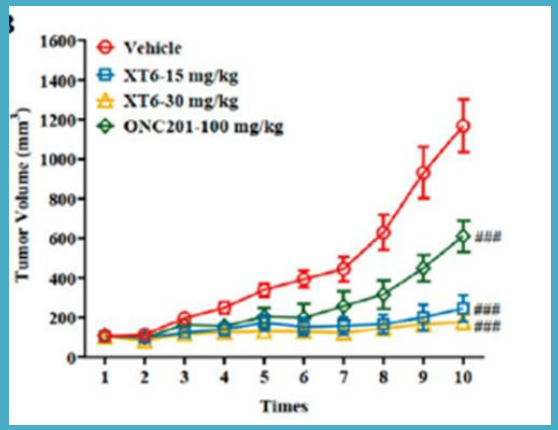
Human ClpP (HsClpP) as a potential anti-cancer target

The human Caseinolytic Protease P (ClpP) protein has been identified as a novel and promising drug target for various hematologic malignancies and solid tumors.

Under normal chaperone-controlled conditions, HsClpP only degrades mis-folded or damaged peptides and proteins in the mitochondria.

Agonists remove the need for the chaperones, and lead to unregulated proteolysis within the mitochondria. This blocks cell growth and proliferation.

Several types of cancers (including breast, colon, pancreas, gliomas) over-express HsClpP and activity is related to expression levels.



Current HsClpP Agonists in clinical trials

The most clinically advanced HsClpP agonist is a small synthetic molecule called ONC-201 (Dordaviprone).

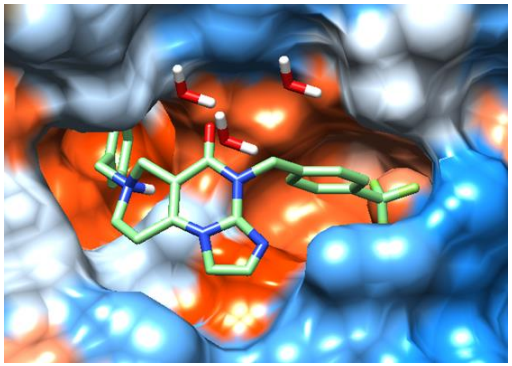
It is currently in a phase III study for a specific type of glioma.

Interestingly, the specific mechanism of action for ONC-201, and structural analogues, was not discovered until 5 years after at it had entered clinical trials.

Clinical derived evidence also supports activation of HsClpP as the mechanism of action.

A more potent analogue of ONC201, ONC206, has also entered phase I/II studies.

ONC201 currently belongs to JAZZ Pharmaceuticals



Project CLIP-CAN (MICINN) (Ref# CPP2023-010755)

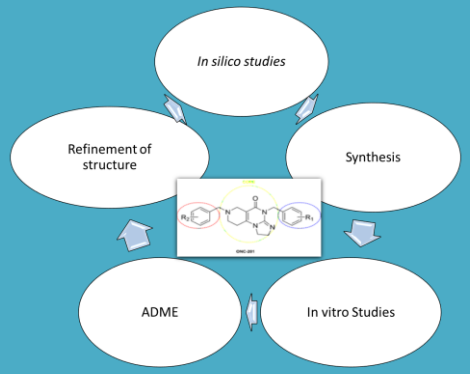
The objective of this project is to identify new, more potent and selective HsClpP agonists that can be designated as clinical candidates for resistant types of cancers.

CEAMED has new families of HsClpP agonists. Several compounds possess superior potencies, selectivity and HLM stability, than either ONC201 or ONC206.

CEAMED SA has registered EP and PCT patent applications for these compounds.

More information about this project can be found at:

www.clip-can.com



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