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tested by in
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discovery was
haphazard.

Nowadays, with
the rapidly
growing field of
proteomics

(study of entire
protein sub-sets
of a cell), a
protease and its

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substrate
repertoire
(degradome) may
be studied in a
complex context
to identify
physiologically
relevant
substrates. The
author Daniel
Ambort describes
step-by-step
first the
principles of

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degradomics and then its application in protease-substrate discovery. Two biological systems, a cell-based (culture medium-derived proteins) and a cell-free (human milk as polysubstrate),

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were used to
find hitherto
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spectrometry
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summary, this
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encompasses a complete description of the realization of degradomics projects.

Proteolysis is an irreversible posttranslational modification affecting each and every protein from its

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biosynthesis to
its degradation.
Limited
proteolysis
regulates
targeting and
activity
throughout the
lifetime of
proteins.
Balancing
proteolysis is
therefore
crucial for

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Control

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and the shut

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endogenous

protease

inhibitors.

Beyond the

protein level,

proteolytic

enzymes are

involved in key

decisions during

development that

determine life

and death - from

single cells to

adult

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individuals. In particular, we are becoming aware of the subtle role that proteases play in signaling events within proteolysis networks, in which the enzymes act synergistically and form

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alliances in a
web-like
fashion.

Proteases come
in different
flavors. At
least five
families of
mechanistically
distinct enzymes
and even more
inhibitor
families are
known to date,

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many family members are still to be studied in detail. We have learned a lot about the diversity of the about 600 proteases in the human genome and begin to understand their physiological

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roles in the
degradome.

However, there
are still many
open questions
regarding their
actions in
pathophysiology.

It is in this
area where the
development of
small molecule
inhibitors as
therapeutic

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agents is
extremely
promising.
Approaching
proteolysis as
the most
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irreversible pos
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protein
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essentially
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where team and
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to the discovery
of more than
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along with a
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associated with

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higher plants
and are among
the most
ubiquitous fungi
in terrestrial
ecosystems. Many
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