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STUART LE GRICE

“THERAPEUTIC TARGETING OF HIV REVERSE TRANSCRIPTASE-ASSOCIATED RIBONUCLEASE H-FUNCTION”

15 February 2011 - 11:00

SARDEGNA RICERCHE

(Loc. Piscinamanna – Edificio 2 - Pula)

Moderator: Prof. Enzo Tramontano, UniCa

Introduction to the cycle of seminars: Patricia Rodriguez-Tomé, CRS4

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The ribonuclease H (RNase H) function of HIV reverse transcriptase (RT) is essential for virus infectivity, and thus provides another opportunity for therapeutic intervention. The contribution of RNase H activity at different stages in proviral DNA synthesis will be summarized, together with single molecule spectroscopy studies that illustrate how the nature of the substrate (a DNA/RNA hybrid) can affect enzyme orientation.

In addition, a National Cancer Institute high throughput screening program has identified two structurally- and mechanistically-distinct classes of HIV RNase H inhibitor. Firstly natural product alpha -hydroxytropolones inhibit catalysis by coordinating divalent metal at the RNase H active site. In contrast, vinylogous ureas, identified from a library of chemical entities, binds in the vicinity of the RNase H active site, functioning as an allosteric inhibitor. The biochemistry, structural biology and in vivo potency of these inhibitor classes, in addition to their impact on enzyme dynamics, will be reviewed.

Information and registration available at www.sardegnareserche.it/agenda/eventi