

**Figure S15.** Autoradiogram of 20% denaturing PAGE, showing the cleavage kinetics of 5'- $^{32}$ P-labelled target RNA (14) by RNase H1 in the native AON (1)/RNA (14), 15-DPPz AON (7) /RNA (14), 15-3T-DPPZ (8) /RNA (14), 15-3T-Cholest AON (10) /RNA (14) and 15-2C-Cholest AON (11) /RNA (14) hybrid duplexes. The kinetics of the control native 15mer AON (1) and double **T** AON (3) with 1 μM and RNA (14) with 0.1μM concentration, used for the calibration of the exact RNase H concentration, are also shown. PDE-Ladder: snake venom PDE ladder. Conditions of cleavage reaction: RNA (0.01 or 0.1 μM) and AONs (1 or 5 μM) in buffer, containing 20 mM Tris-HCl (pH 8.0), 20 mM KCl, 10 mM MgCl<sub>2</sub> and 0.1 mM DTT at 21 °C, 0.06 U of RNase H. Total reaction volume is 30 μl. (See Materials and Methods section for full experimental details.)