

**Figure S3: *In vitro* characterization of StCsm complexes targeting *tdgf1* transcript. Related to Figure 4.** (A) Coomassie blue-stained SDS-PAGE of purified StCsm complexes. M - protein mass marker. (B) Denaturing PAGE analysis of crRNA co-purifying with the StCsm complexes. 0 – crRNA from wt StCsm(S3) used as marker. (C) RNA cleavage activity *in vitro* by single and multiple *tdgf1*-targeting StCsm complexes. Depletion of *in vitro* transcribed radioactively 5'-labeled target RNAs measured in 45 minutes after RNA cleavage reaction initiation with  $Mg^{2+}$ . Cleavage reactions were performed at 28°C and contained 8 nM of 5'-radiolabeled RNA, 160 nM StCsm and 10mM Mg-acetate. For wt-StCsm(*tdgf1*<sup>167</sup>) only *tdgf1*<sup>167</sup> RNA and NS RNA substrates were used (Table S2). Data are represented as mean  $\pm$  SEM. (D) DNA cleavage *in vitro* by wt, dRNase, and dDNase StCsm(*tdgf1*<sup>167,174,154,181</sup>) complexes in the presence of the *tdgf1*<sup>167</sup> RNA. Cleavage reactions were performed at 28°C and contained 1 nM M13mp18 ssDNA, 7.5 nM StCsm, 10 mM  $MnCl_2$  and 7.5 nM *tdgf1*<sup>167</sup> RNA. Reactions were initiated by addition of  $Mn^{2+}$ . Products were analyzed on agarose gel.

