

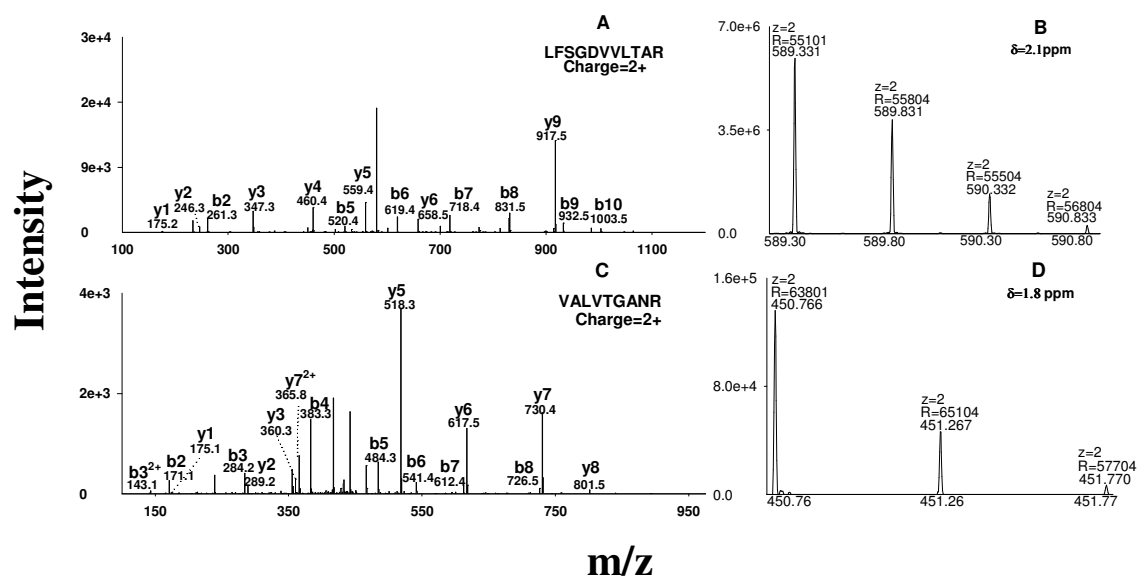
**(A) Carbonyl reductase 1**

|     |            |            |            |             |            |
|-----|------------|------------|------------|-------------|------------|
| 1   | MSSGIHVALV | TGGNKGIGLA | IVRDLCLRFS | GDVVLTDARDV | TRGQAAVQQL |
| 51  | QAEGLSPRFH | QLDIDDLQSI | RALRDFLRKE | YGGLDVLVNN  | AGIAFKVADP |
| 101 | TPFHIAEVT  | MKTNFFGTRD | VCTELLPLIK | PQGRVVNVSS  | IMSVRALKSC |
| 151 | SPELQQKFRS | ETITEEELVG | LMNKFVEDTK | KGVHQKEGWP  | SSAYGVTKIG |
| 201 | VTVLSRIHAR | KLSEQRKGDK | ILLNACCPGW | VRTDMAGPKA  | TKSPEEGAET |
| 251 | PVYLALLPPD | AEGPHGQFVS | EKRVEQW    |             |            |

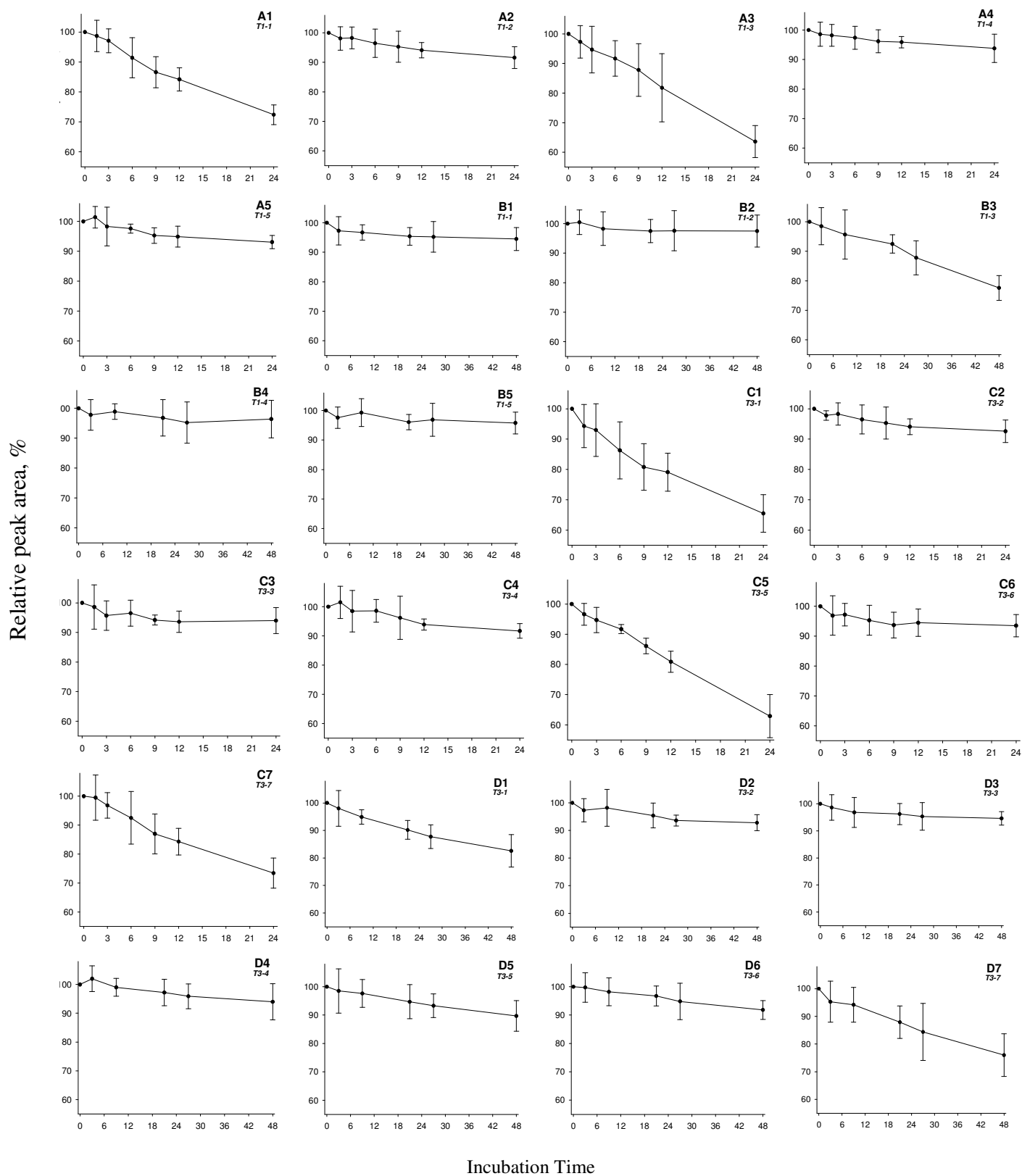
**(B) Carbonyl reductase 3**

|     |            |            |            |             |            |
|-----|------------|------------|------------|-------------|------------|
| 1   | MSSCSRVALV | TGANRGIGLA | IARELCRQFS | GDVVLTDARDV | ARGQAAVQQL |
| 51  | QAEGLSPRFH | QLDIDDLQSI | RALRDFLRKE | YGGLNVLVNN  | AAVAFKSDDP |
| 101 | MPFDIAEMT  | LKTNFFATR  | MCNELLPIMK | PHGRVVNISS  | LQCLRAFENC |
| 151 | SEDLQERFHS | ETLTEGDLVD | LMKKFVEDTK | NEVHEREGWP  | NSPYGVSKLG |
| 201 | VTVLSRILAR | RLDEKRKADR | ILVNACCPGP | VKTDMDGKDS  | IRTVEEGAET |
| 251 | PVYLALLPPD | ATEPQGQLVH | DKVVQNW    |             |            |

**SI Figure 1.** The sequence coverage of CBR1 and CBR3, analyzed from tryptic digests of both proteins using nano-LC/LTQ/Orbitrap. The residues in red denote the sequence identified with high confidence, while those in black are in the domains that were not. Collision induced dissociation (CID) was used for peptide fragmentation. Criteria for identification were highly stringent, including high thresholds for Xcorr, 10 ppm for precursor m/z tolerance and a peptide probability >95% (*EXPERIMENTAL* section)



**SI Figure 2.** Representative MS spectra for the identification of peptides derived from CBR1 and CBR3, using a nano-LC/LTQ/Orbitrap. (A) CID spectrum of peptide LFSGDVLTAR (T1-5 from CBR1); (B) confirmation of the identification of T1-5 by accurate precursor measurement using the Orbitrap; (C) CID spectrum of peptide VALVTGANR (T3-4 from CBR3); (D) confirmation of the identification of T3-4 using the Orbitrap. Abbreviation:  $\delta$ , mass error in ppm.



**SI Figure 3.** Time-dependence of the stability of the candidate peptides derived from CBR1 at (A1-A5) 37 °C and pH=8.5 for 24 h and (B1-B5) 6 °C and pH=2.5 for 48h. Stability of the candidate peptides derived from CBR3 at (C1-C7) 37 °C and pH=8.5 for 24 h and (D1-D7) 6 °C and pH=2.5 for 48h. The evaluations were performed in triplicate.