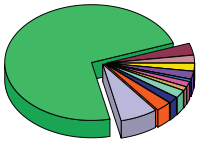
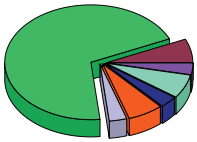
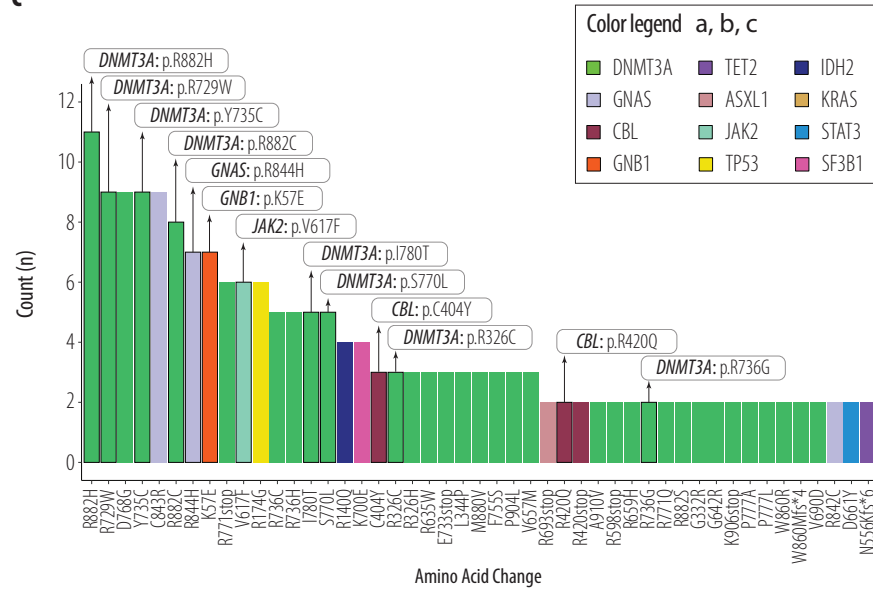
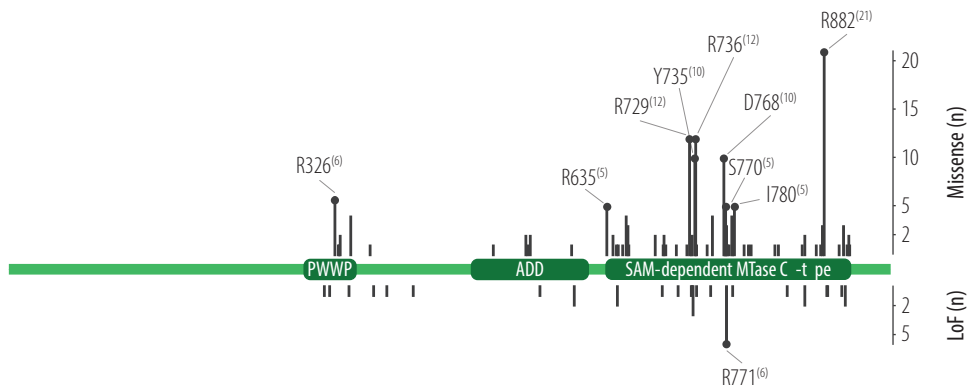
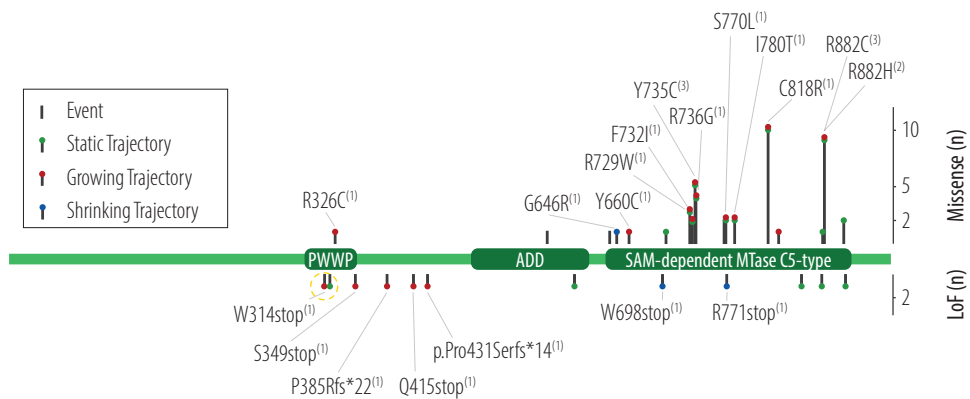
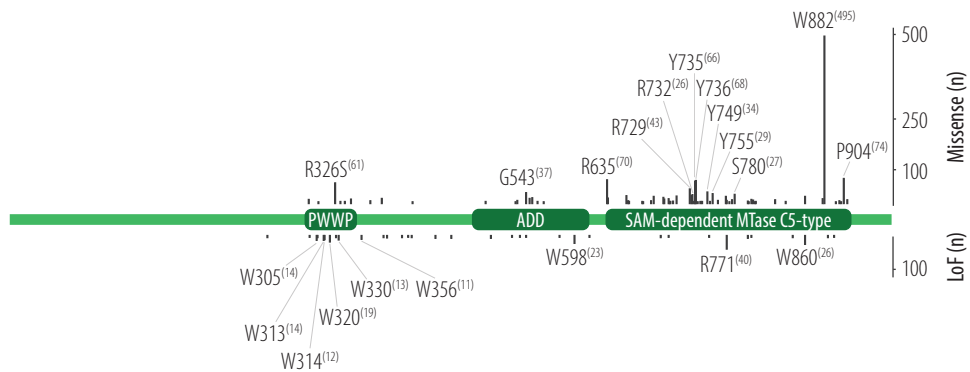


**a****b****c****d****e****f**

**File S5. CHDMs identified in the single- and multiple timepoint datasets and comparison to literature.** **(a)** The gene distribution of identified CHDMs in the single-timepoint dataset (total number of CHDMs=273). **(b)** The gene distribution of growing CHDM trajectories in the multiple-timepoint dataset (total number of growing trajectories=30). **(c)** The number of CHDMs resulting in specific amino acid changes in the single-timepoint dataset at the protein level. Labels indicate CHDMs that have been defined as growing trajectories in our multiple-timepoint dataset. **(d)** Amino acid changes caused by DNMT3A mutations in our single-timepoint dataset annotated on a schematic visualization of the DNMT3A protein. Mutations affecting the same amino acid residue five or more times have been annotated and the label specifies the reference amino acid, position and number of mutations in superscript. Labels: R326<sup>(6)</sup> = R326H (n=3), R326C (n=3); R635<sup>(5)</sup> = R635W (n=3), R635Q (n=1), R635L (n=1); R729<sup>(12)</sup> = R729W (n=9), R729Q (n=1), R729G (n=1), R729L (n=1); Y735<sup>(10)</sup> = Y735C (n=9), Y735S (n=1); R736<sup>(12)</sup> = R736C (n=5), R736H (n=5), R736G (n=2); D768<sup>(10)</sup> = D768G (n=9), D768V (n=1); R771<sup>(6)</sup> = R771stop (n=6); R882<sup>(21)</sup> = R882H (n=11), R882C (n=8), R882S (n=2). **(e)** Amino acid changes caused by DNMT3A mutations in our multiple-timepoint dataset annotated on a schematic visualization of DNMT3A protein. CHDMs that have been categorized as trajectories have been given a coloured dot: red for growing (with a dashed yellow circle for ‘late-appearing clone’), green for static and blue for shrinking. Labels constitute the reference amino acid in single letter code, position, and alternative amino acid, and are provided only for growing and shrinking trajectories (as represented by the number in superscript), and not for static trajectories or events (with the exception of ‘late-appearing clone’). **(f)** DNMT3A mutations (amino acid changes) observed at least five times in literature annotated on a schematic visualization of DNMT3A protein. Missense mutations observed >25 times, and LoF mutations observed >10 times have been annotated and the label specifies the reference amino acid, position and number of calls in superscript. For a complete table of all CHDMs observed in literature, see File S3, table 3a. DNMT3A protein annotation source: <https://www.uniprot.org/uniprot/Q9Y6K1>.