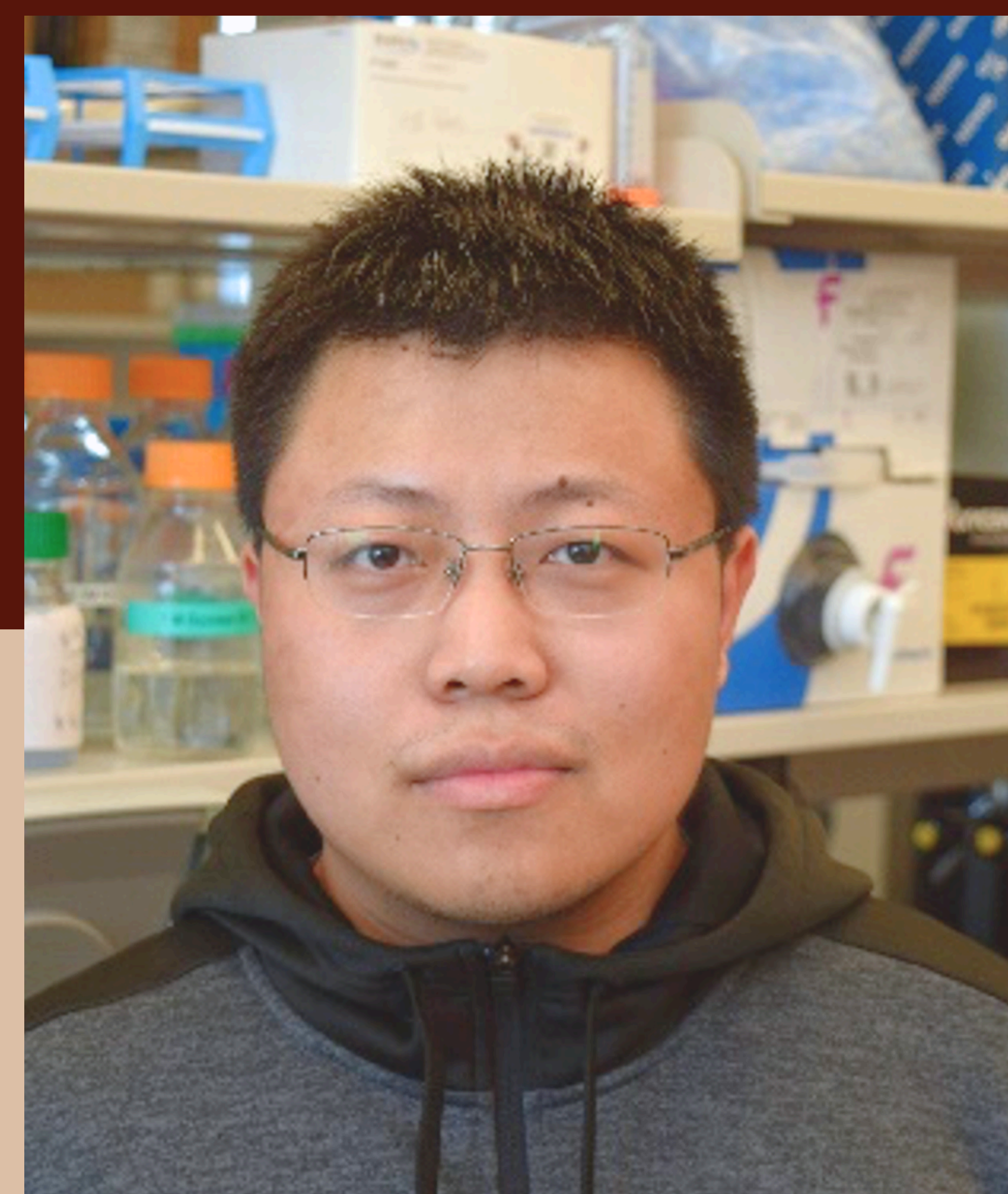




Decoding the Monoamine-Modified Proteome: From Chemical Biology to Cancer Therapy

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Abstract: Transglutaminase (TG)-catalyzed monoaminylation is an emerging protein post translational modification (PTM) that has been found highly related to diverse human diseases. This unique PTM is based on the formation of an isopeptide bond between the γ -carboxyl group of protein glutamine residues and primary amine groups of monoamine metabolites (including serotonin, dopamine, histamine, etc.). The fifth amino acid residue (i.e., glutamine) of histone H3 (H3Q5) has been shown to serve as a primary monoaminylation site by human transglutaminase 2 (TG2), which plays significant epigenetic roles for regulating gene transcription in cancer and nerve cells. Our recent studies discovered that the dynamics of protein monoaminylation (including installation, removal, and replacement) were solely regulated by one enzyme, TG2, via a reversible transamidation reaction, where the substrate glutamine formed a reactive thioester intermediate with TGM2's catalytic cysteine. The high enzyme promiscuity of TG2 enables the application of chemical biology tools for profiling the monoamine-modified proteome. A series of chemical biology approaches have been developed by my lab and unveiled the uncharted monoaminylation proteome in tumor cells (such as histaminylated histone H2AX and norepinephrinylated SHP2), suggesting its novel pathological roles in cancer development and therapeutic potential.

Wednesday, September 16 | 2:00pm-3:15pm | Science Hall 126 & Zoom

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