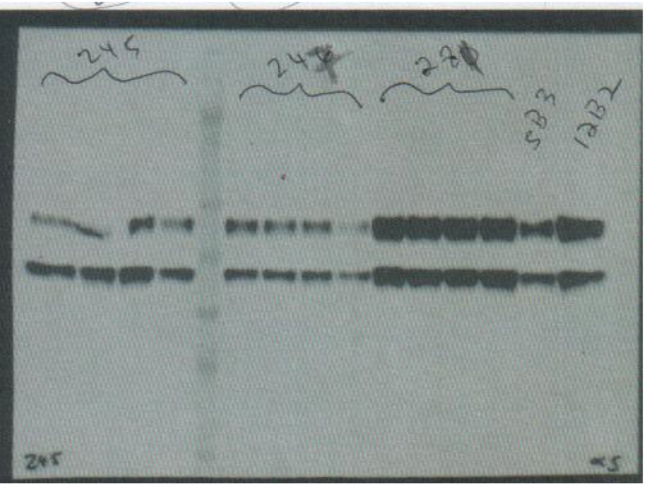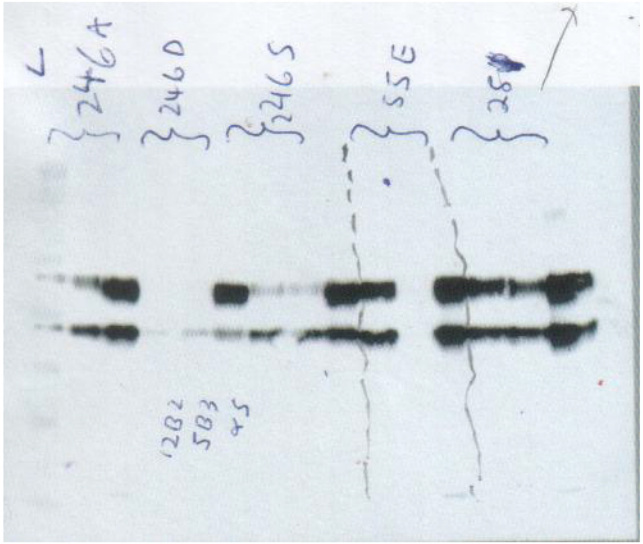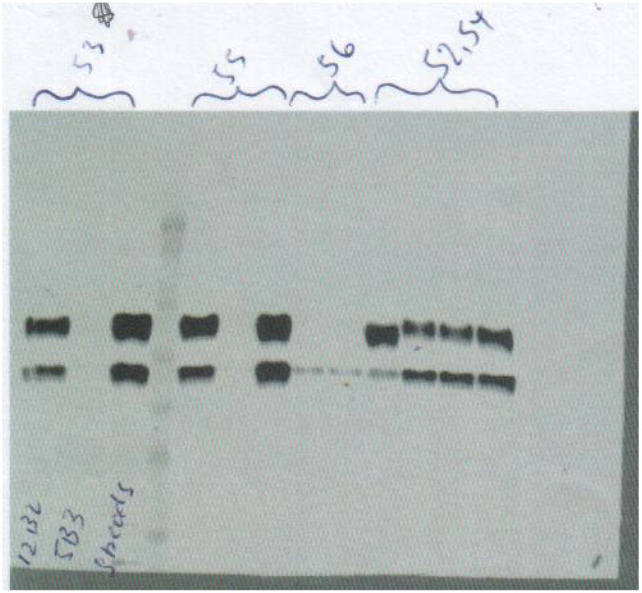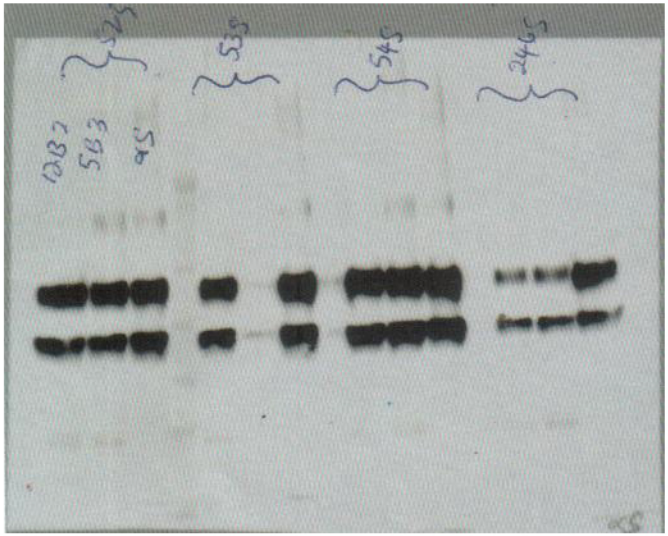Extended Data 4