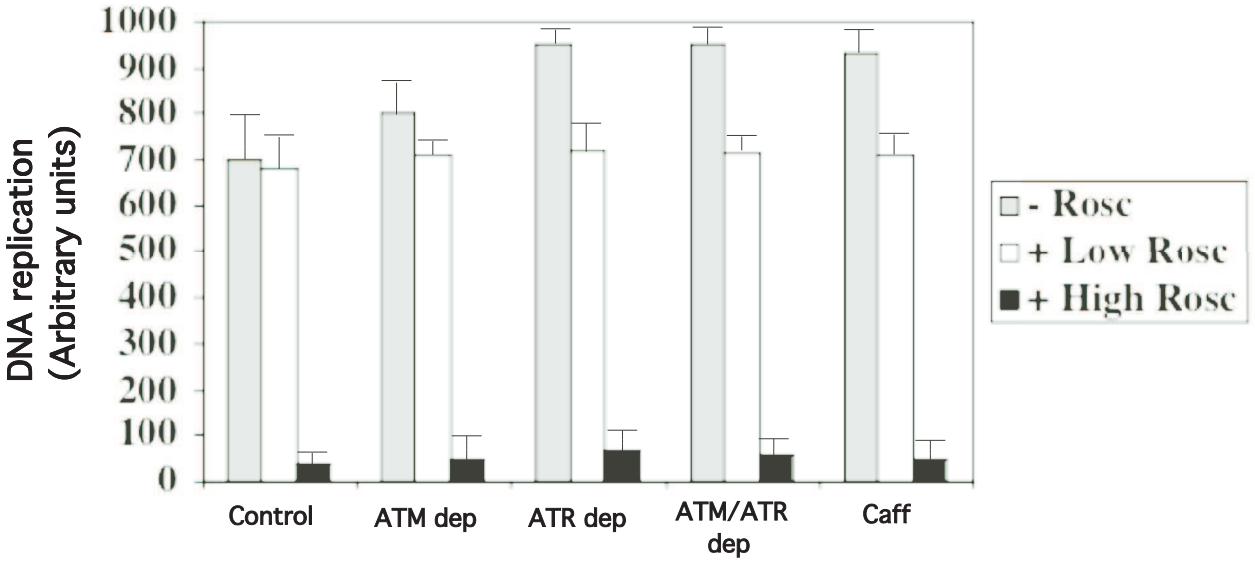Supplemental Fig 2