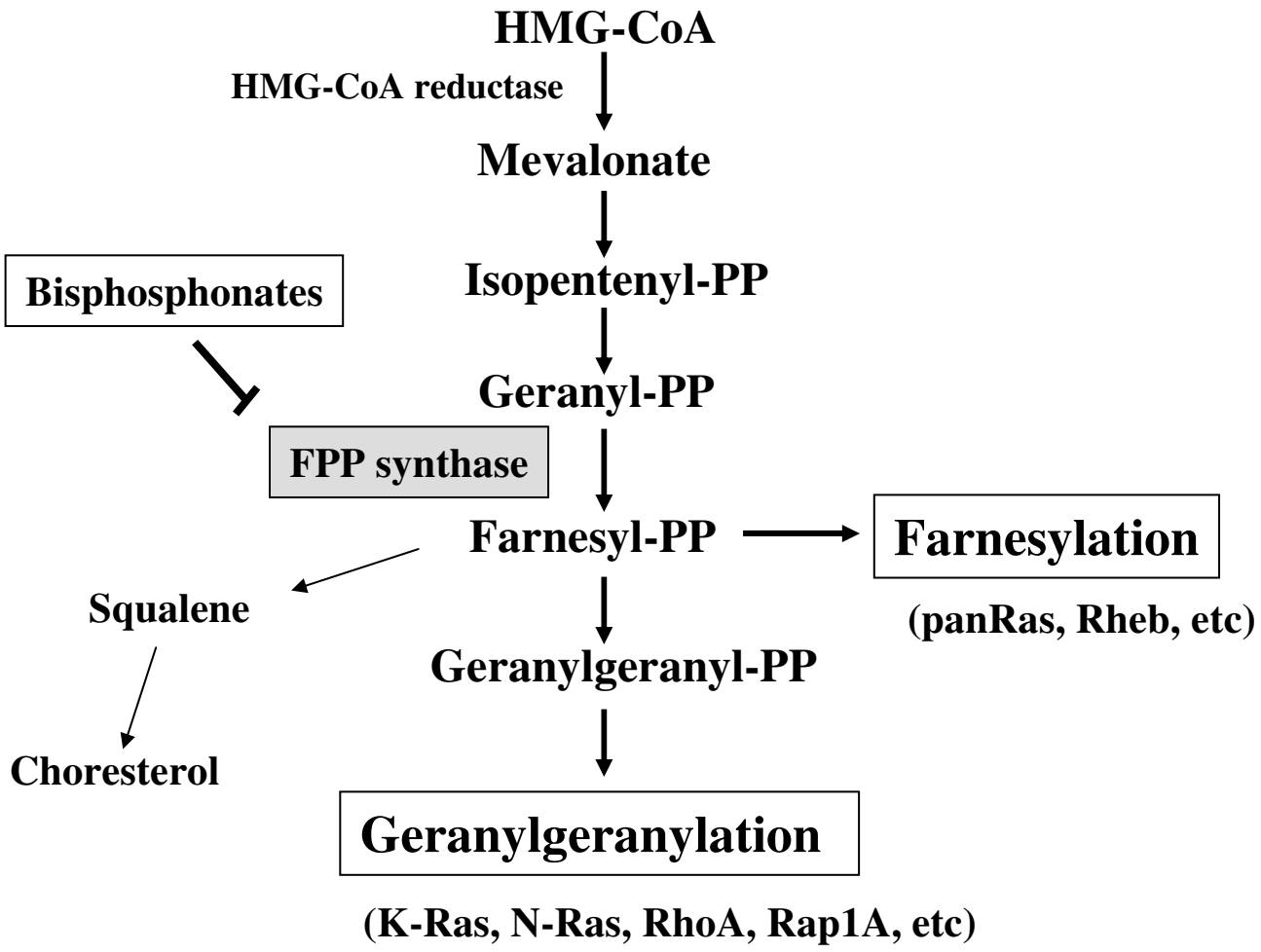Supplemental Fig 1