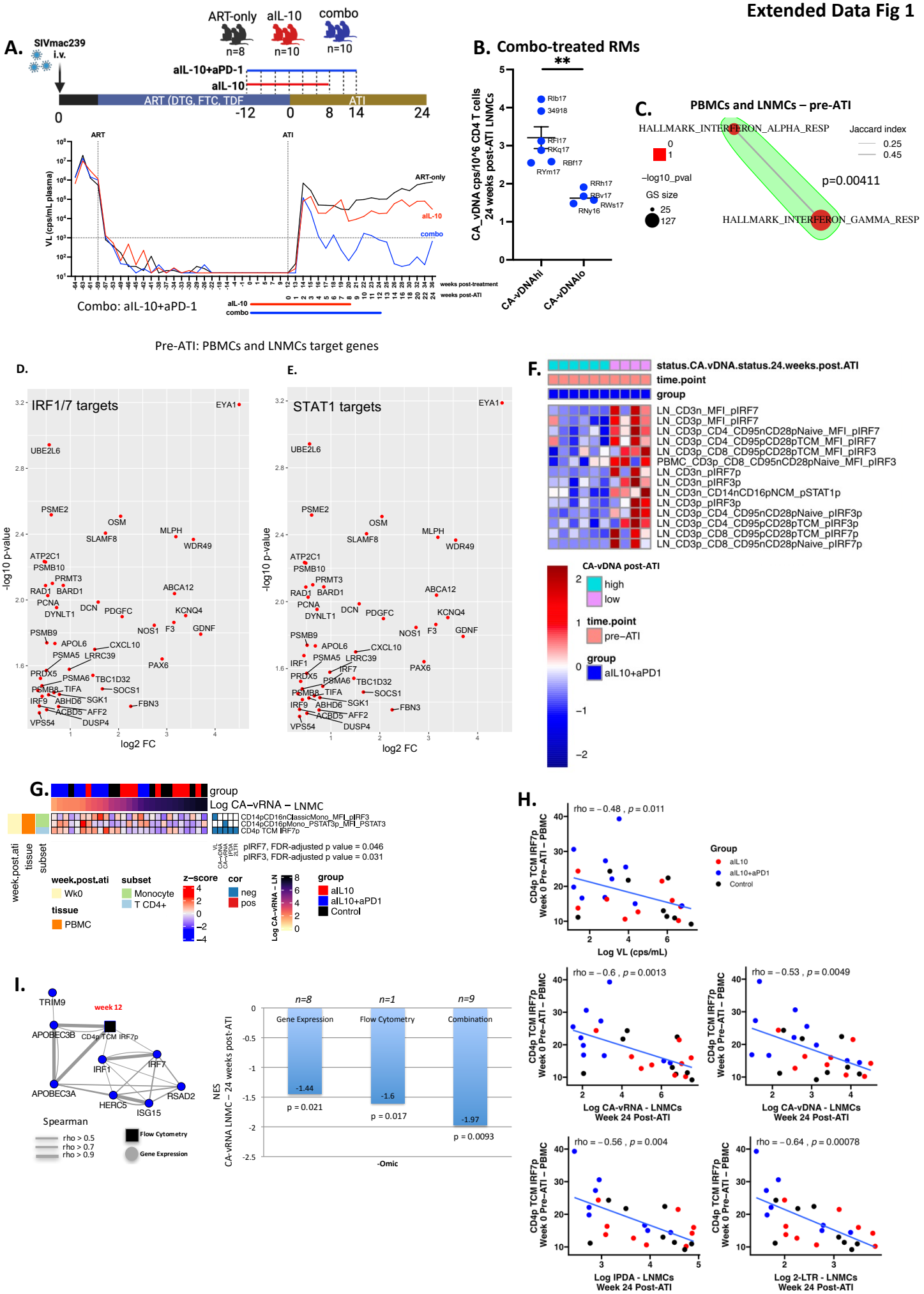Extended Data Fig 1