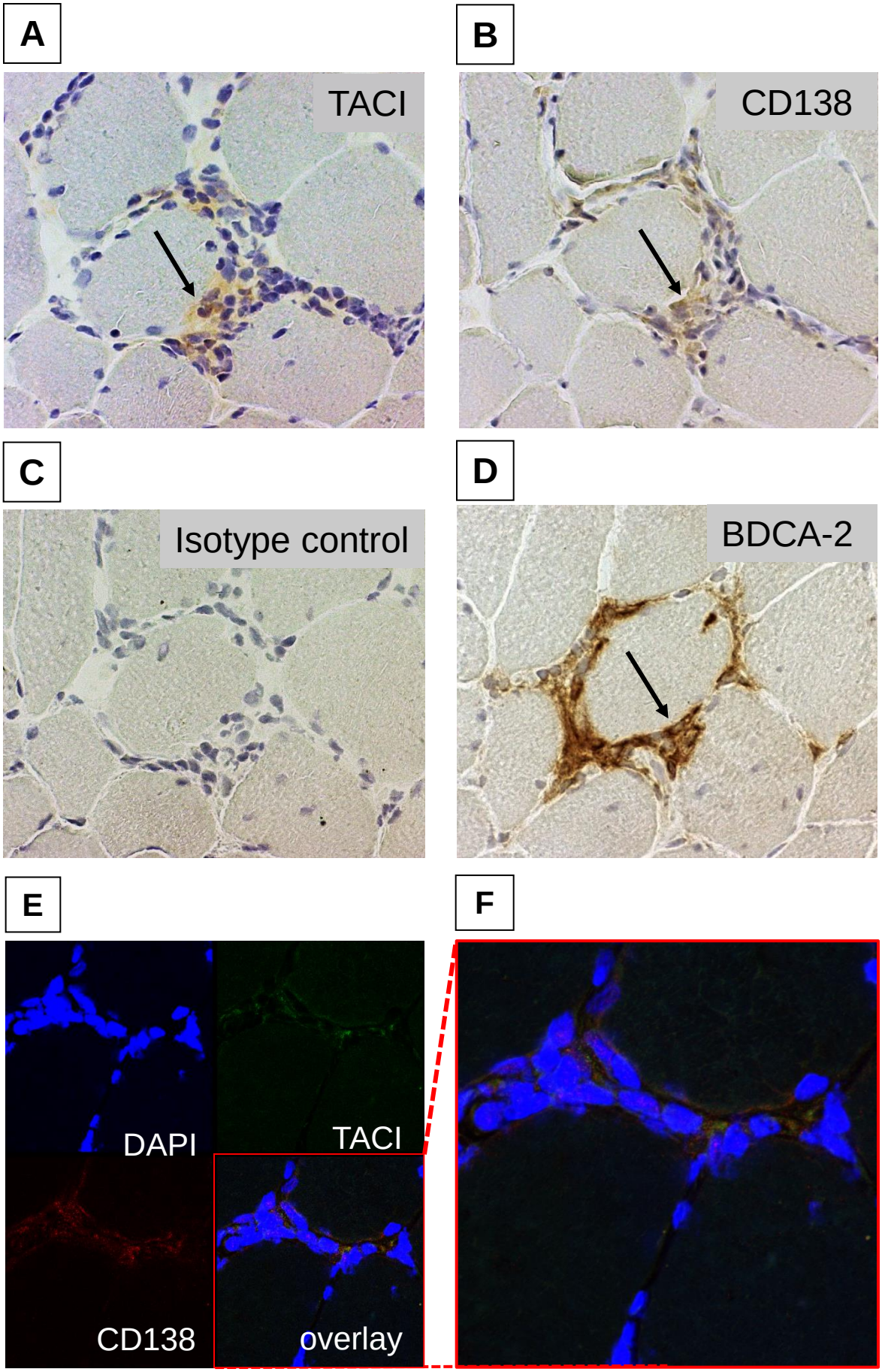Additional figure 3