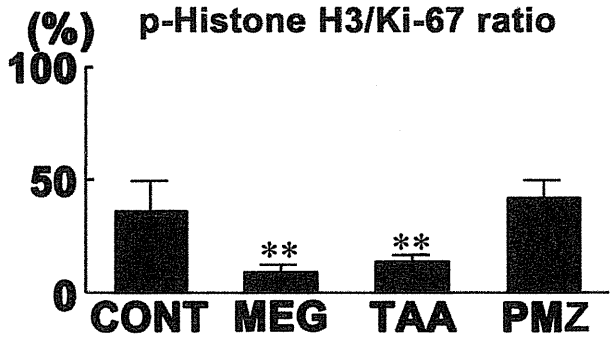

Fig. 5. p-Histone $H3^+/Ki\text{-}67^+$ cell ratio in the liver of rats at day 28 after treatment with MEG, TAA or PMZ. The graph shows p-Histone $H3^+$ cell ratio of hepatocytes per $Ki\text{-}67^+$ cells counted in 10 animals in each group. Values represent mean + SD. ** $P < 0.01$ vs. the untreated controls (Steel's test).

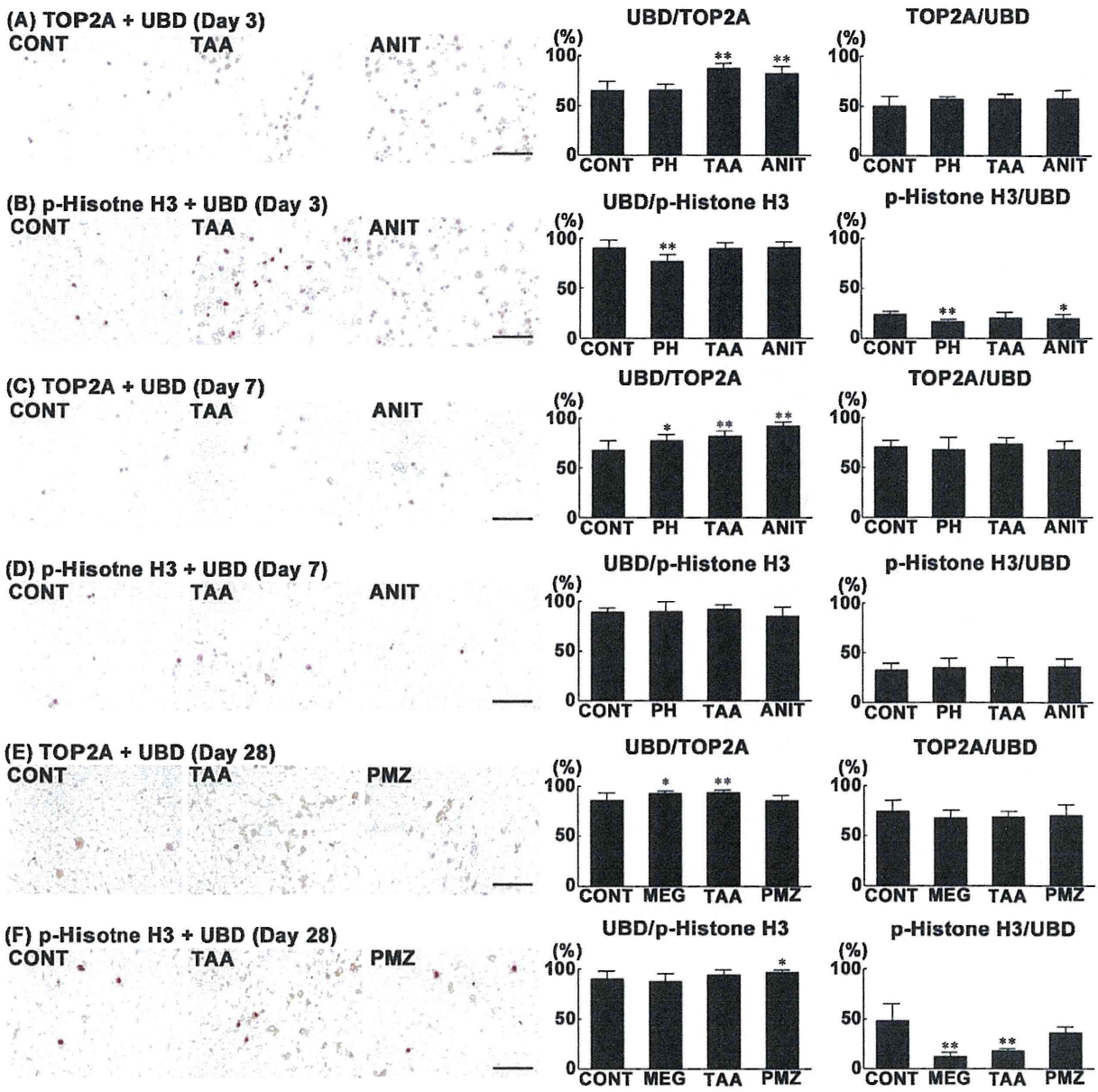

Fig. 6. Distribution of immunoreactive cell populations of TOP2A co-expressing UBD (UBD/TOP2A), UBD co-expressing TOP2A (TOP2A/UBD), p-Histone H3 co-expressing UBD (UBD/p-Histone H3) or UBD co-expressing p-Histone H3 (p-Histone H3/UBD) in the liver of rats at days 3, 7 and 28. Photomicrographs show the distribution of UBD/TOP2A, TOP2A/UBD, UBD/p-Histone H3, and p-Histone H3/UBD in the liver of untreated controls (A–F), animals treated with TAA or ANIT (A, B, C, D), and animals treated with TAA or PMZ (E, F). The immunoreactivity of UBD (cytoplasm), and p-Histone H3 (nucleus) or TOP2A (nucleus) is visualized as brown and red, respectively. The graphs show the UBD-positive cell ratio (%) per total liver cells immunoreactive with TOP2A or p-Histone H3, and the TOP2A or p-Histone H3-positive cell ratio (%) per total liver cells immunoreactive with UBD counted in 10 animals in each group. Values represent mean + SD. (A) UBD/TOP2A and TOP2A/UBD, (B) UBD/p-Histone H3 and p-Histone H3/UBD (day 3), (C) UBD/TOP2A and TOP2A/UBD (day 7), (D) UBD/p-Histone H3 and p-Histone H3/UBD (day 7), (E) UBD/ TOP2A and TOP2A/UBD (day 28), (F) UBD/p-Histone H3 and p-Histone H3/UBD (day 28). Bar = 100 μm. *, ** $P < 0.05$, 0.01, respectively, vs. untreated controls (Dunnett's or Steel's test).

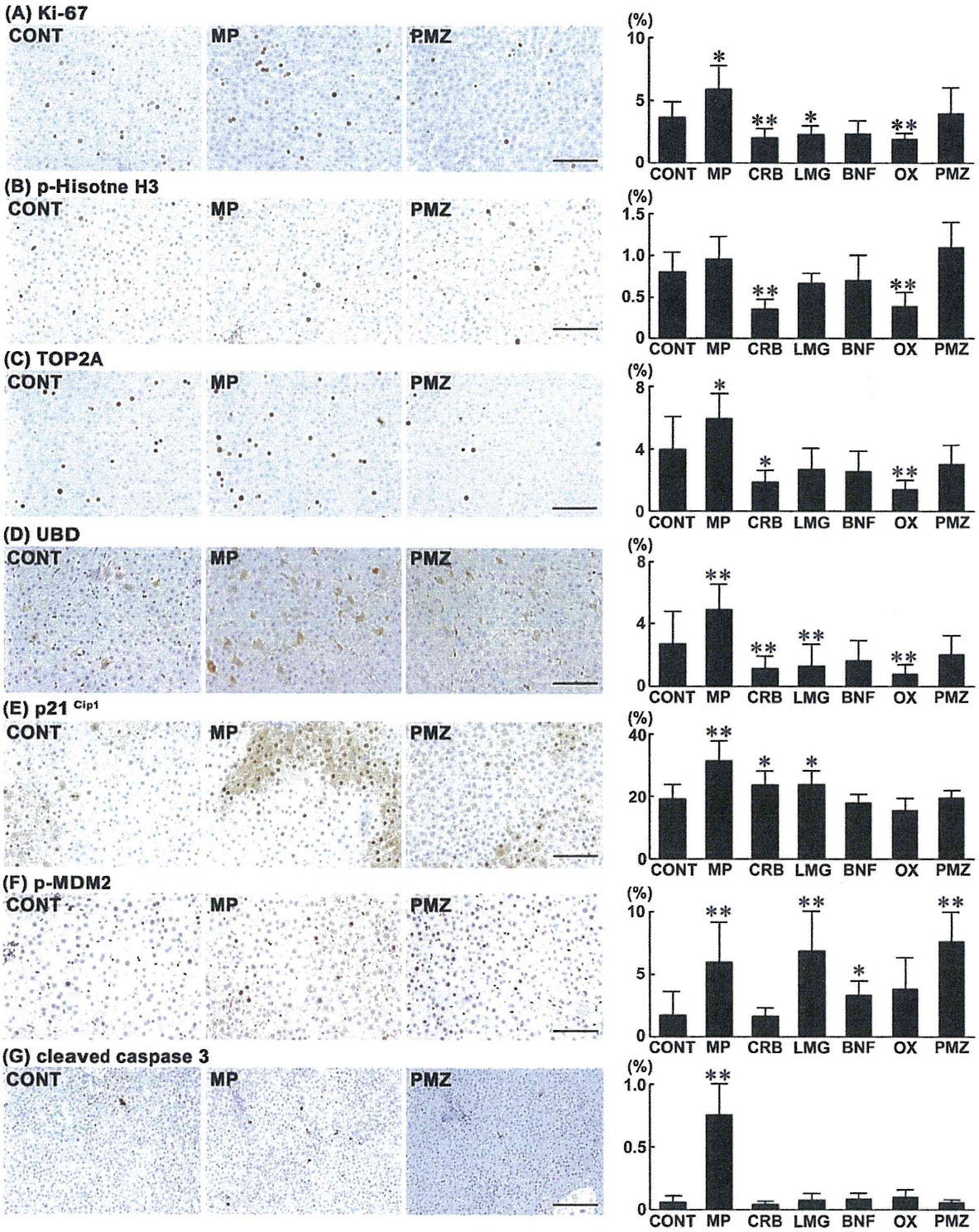

Fig. 7. Distribution of Ki-67$^+$, p-Histone H3$^+$, TOP2A$^+$, UBD$^+$, p21^{Cip1+}, p-MDM2$^+$ and cleaved caspase 3$^+$ cells in the liver of rats at day 7 after treatment with hepatocarcinogens, hepatocarcinogenic promoters or non-carcinogenic hepatotoxicants. Photomicrographs show the distribution of Ki-67$^+$, p-Histone H3$^+$, TOP2A$^+$, UBD$^+$, p21^{Cip1+}, p-MDM2$^+$ and cleaved caspase 3$^+$ cells in the liver of representative cases from untreated controls and animals treated with MP or PMZ. The graphs show positive cell ratios of hepatocytes per total cells counted in 10 animals of each group. Values represent mean + SD. (A) Ki-67, (B) p-Histone H3, (C) TOP2A, (D) UBD, (E) p21^{Cip1}, (F) p-MDM2, and (G) cleaved caspase 3. Bar = 100 μm (A–F) or 200 μm (G). * $P < 0.05$, ** $P < 0.01$ vs. untreated controls (Dunnett's or Steel's test).

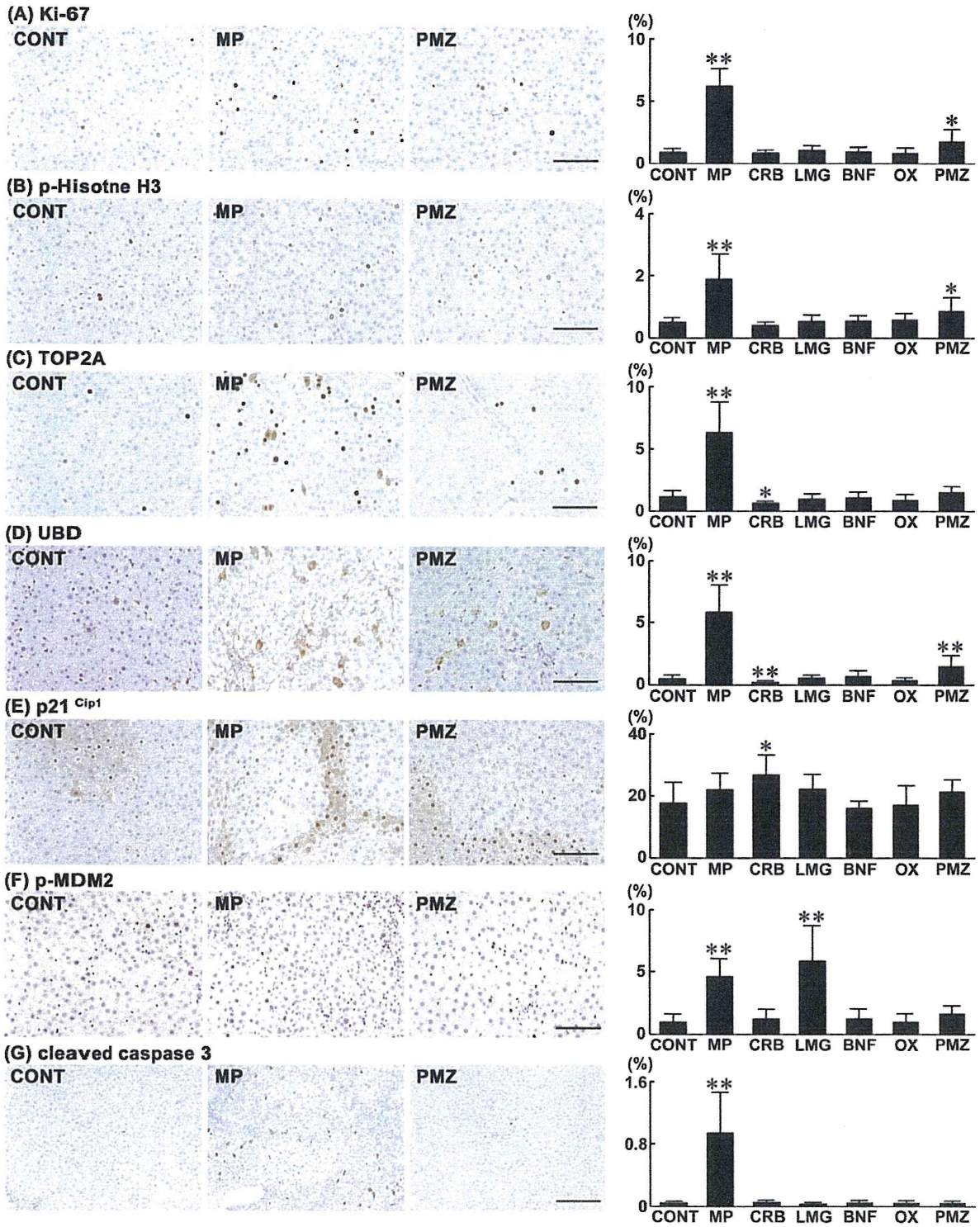

Fig. 8. Distribution of Ki-67$^+$, p-Histone H3$^+$, TOP2A$^+$, UBD$^+$, p21^{Cip1+}, p-MDM2$^+$ and cleaved caspase 3$^+$ cells in the liver of rats at day 28 after treatment with hepatocarcinogens, hepatocarcinogenic promoters or non-carcinogenic hepatotoxicants. Photomicrographs show the distribution of Ki-67$^+$, p-Histone H3$^+$, TOP2A$^+$, UBD$^+$, p21^{Cip1+}, p-MDM2$^+$ and cleaved caspase 3$^+$ cells in the liver of representative cases from untreated controls and animals treated with MP or PMZ. The graphs show positive cell ratios of hepatocytes per total cells counted in 10 animals of each group. Values represent mean + SD. (A) Ki-67, (B) p-Histone H3, (C) TOP2A, (D) UBD, (E) p21^{Cip1}, (F) p-MDM2, and (G) cleaved caspase 3. Bar = 100 μm (A–F) or 200 μm (G). * $P < 0.05$, ** $P < 0.01$ vs. untreated controls (Dunnett's or Steel's test).

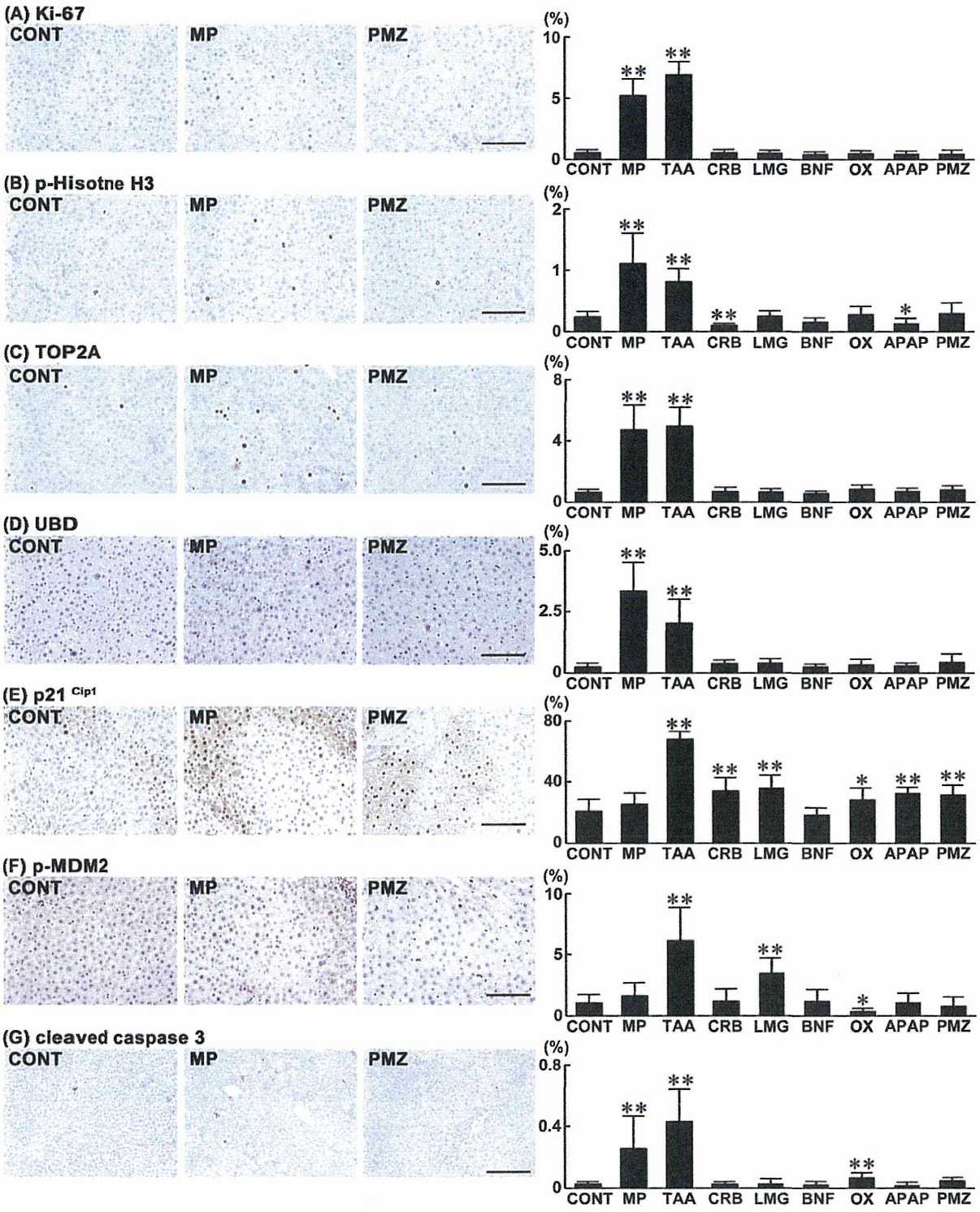

Fig. 9. Distribution of Ki-67$^+$, p-Histone H3$^+$, TOP2A$^+$, UBD$^+$, p21^{Cip1+}, p-MDM2$^+$ and cleaved caspase 3$^+$ cells in the liver of rats at day 90 after treatment with hepatocarcinogens, hepatocarcinogenic promoters or non-carcinogenic hepatotoxicants. Photomicrographs show the distribution of Ki-67$^+$, p-Histone H3$^+$, TOP2A$^+$, UBD$^+$, p21^{Cip1+}, p-MDM2$^+$ and cleaved caspase 3$^+$ cells in the liver of representative cases from untreated controls and animals treated with MP or PMZ. The graphs show positive cell ratios of hepatocytes per total cells counted in 10 animals of each group. Values represent mean + SD. (A) Ki-67, (B) p-Histone H3, (C) TOP2A, (D) UBD, (E) p21^{Cip1}, (F) p-MDM2, and (G) cleaved caspase 3. Bar = 100 μm (A–F) or 200 μm (G). * $P < 0.05$, ** $P < 0.01$ vs. untreated controls (Dunnett's or Steel's test).

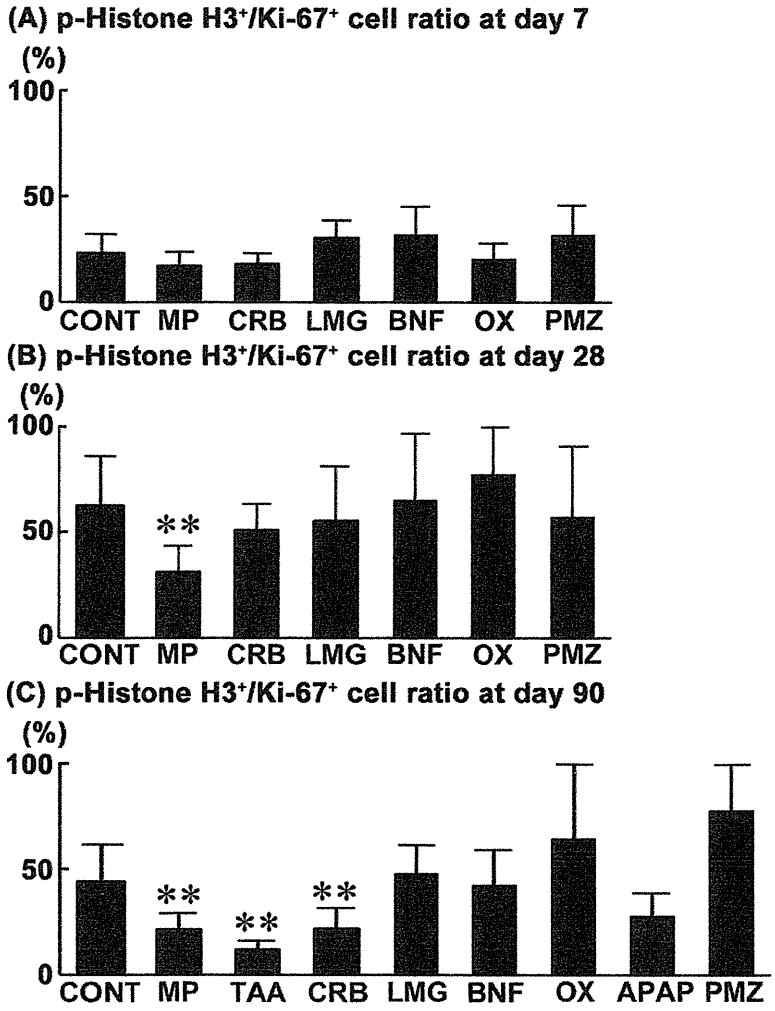

Fig. 10. p-Histone $H3^+/Ki\text{-}67^+$ cell ratio in the liver of rats at day 7, 28 and 90 after treatment with hepatocarcinogens, hepatocarcinogenic promoters and non-carcinogenic hepatotoxicants. The graphs show the p-Histone $H3^+$ cell ratio of hepatocytes per number of $Ki\text{-}67^+$ cells counted in 10 animals of each group. Values represent mean + SD. (A) p-Histone $H3^+/Ki\text{-}67^+$ cell ratio at day 7, (B) p-Histone $H3^+/Ki\text{-}67^+$ cell ratio at day 28, and (C) p-Histone $H3^+/Ki\text{-}67^+$ cell ratio at day 90. ** $P < 0.01$ vs. untreated controls (Steel's test).

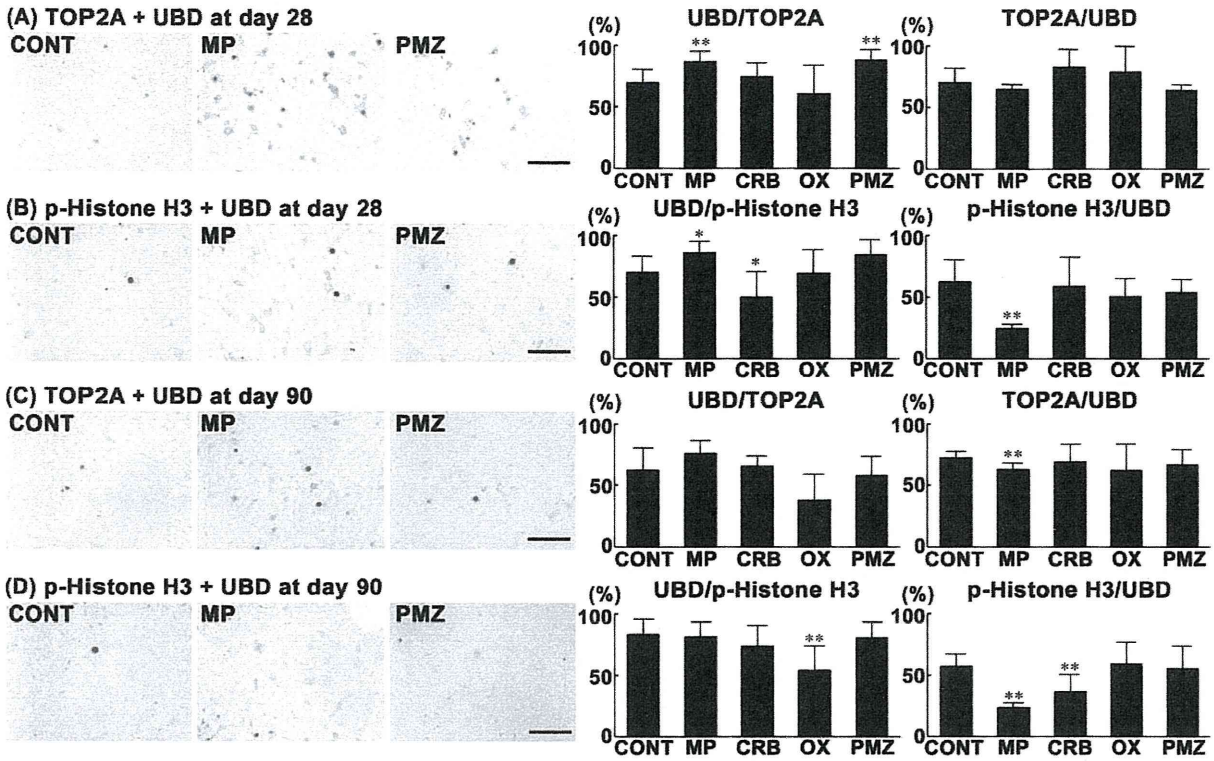

Fig. 11. Distribution of cell populations co-expressing TOP2A and UBD (UBD/TOP2A), UBD and TOP2A (TOP2A/UBD), p-Histone H3 and UBD (UBD/p-Histone H3), or UBD and p-Histone H3 (p-Histone H3/UBD) in the liver of rats at days 28 and 90. Photomicrographs show the distribution of UBD/TOP2A, TOP2A/UBD, UBD/p-Histone H3 and p-Histone H3/UBD in the liver of representative cases from untreated controls and animals treated with MP or PMZ. The immunoreactivity of UBD (cytoplasm), and p-Histone H3 (nucleus) or TOP2A (nucleus) is visualized as brown and red, respectively. The graphs show the UBD-positive cell ratio (%) per total liver cells immunoreactive to TOP2A or p-Histone H3, and the TOP2A or p-Histone H3-positive cell ratio (%) per total liver cells immunoreactive to UBD counted in 10 animals of each group. Values represent mean + SD. (A) UBD/TOP2A and TOP2A/UBD (day 28), (B) UBD/p-Histone H3 and p-Histone H3/UBD (day 28), (C) UBD/TOP2A and TOP2A/UBD (day 90), (D) UBD/p-Histone H3 and p-Histone H3/UBD (day 90). Bar = 100 μm. *, ** $P < 0.05$, 0.01, respectively, vs. untreated controls (Dunnett's or Steel's test).

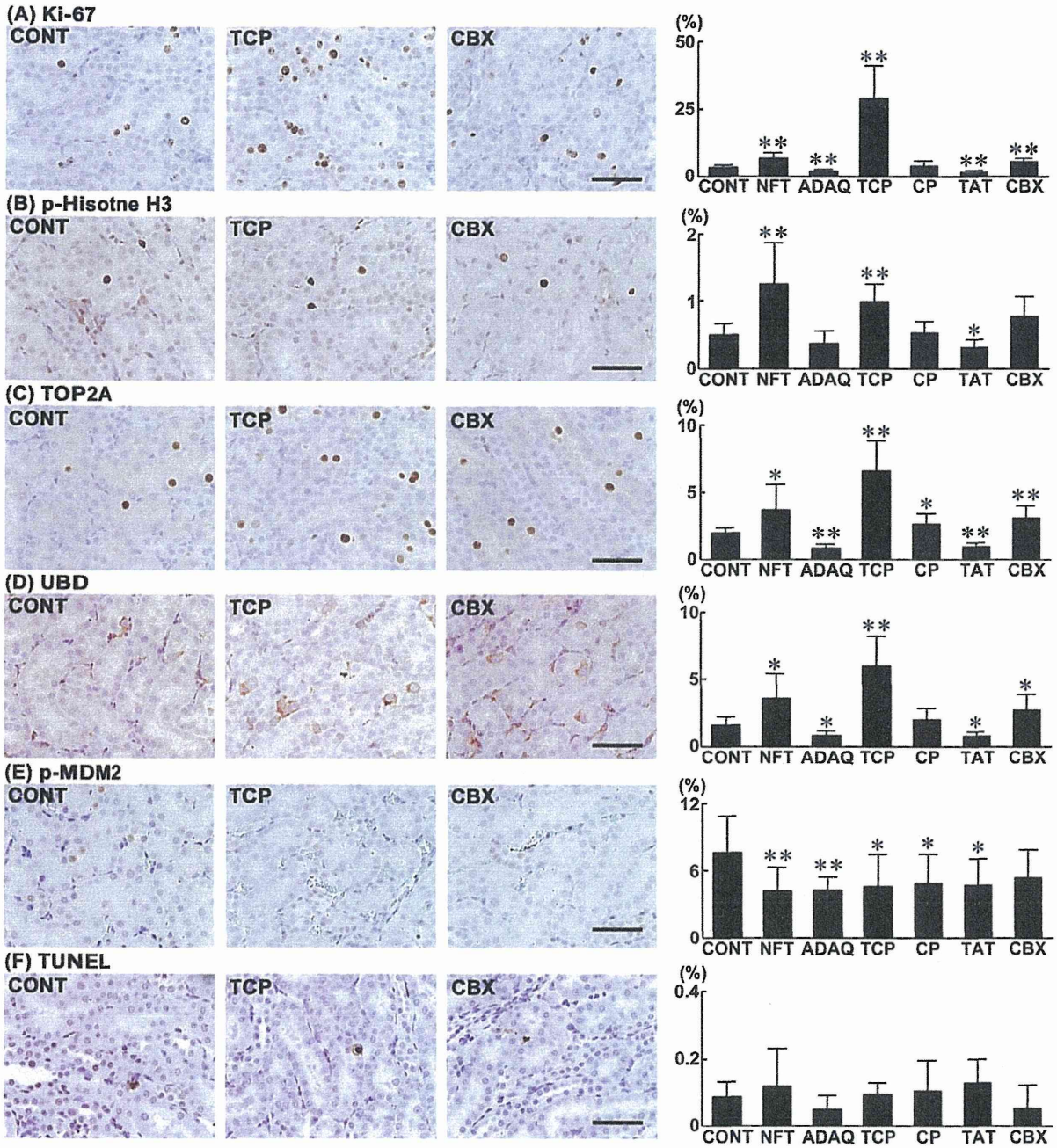

Fig. 12. Distribution of Ki-67$^+$, p-Histone H3$^+$, TOP2A$^+$, UBD$^+$, p-MDM2$^+$, and TUNEL$^+$ cells in the OSOM of rats at day 3 after treatment with renal carcinogens or non-carcinogenic renal toxicants. Photomicrographs show the distribution of Ki-67$^+$, p-Histone H3$^+$, TOP2A$^+$, UBD$^+$, p-MDM2$^+$, and TUNEL$^+$ cells in the OSOM of representative cases from untreated controls and animals treated with TCP or CBX. The graphs show positive cell ratios of renal tubular epithelial cells per total cells counted in 10 animals of each group. Values represent mean + SD. (A) Ki-67, (B) p-Histone H3, (C) TOP2A, (D) UBD, (E) p-MDM2, and (F) TUNEL. Bar = 50 μm. * $P < 0.05$, ** $P < 0.01$ vs. untreated controls (Dunnett's or Steel's test).

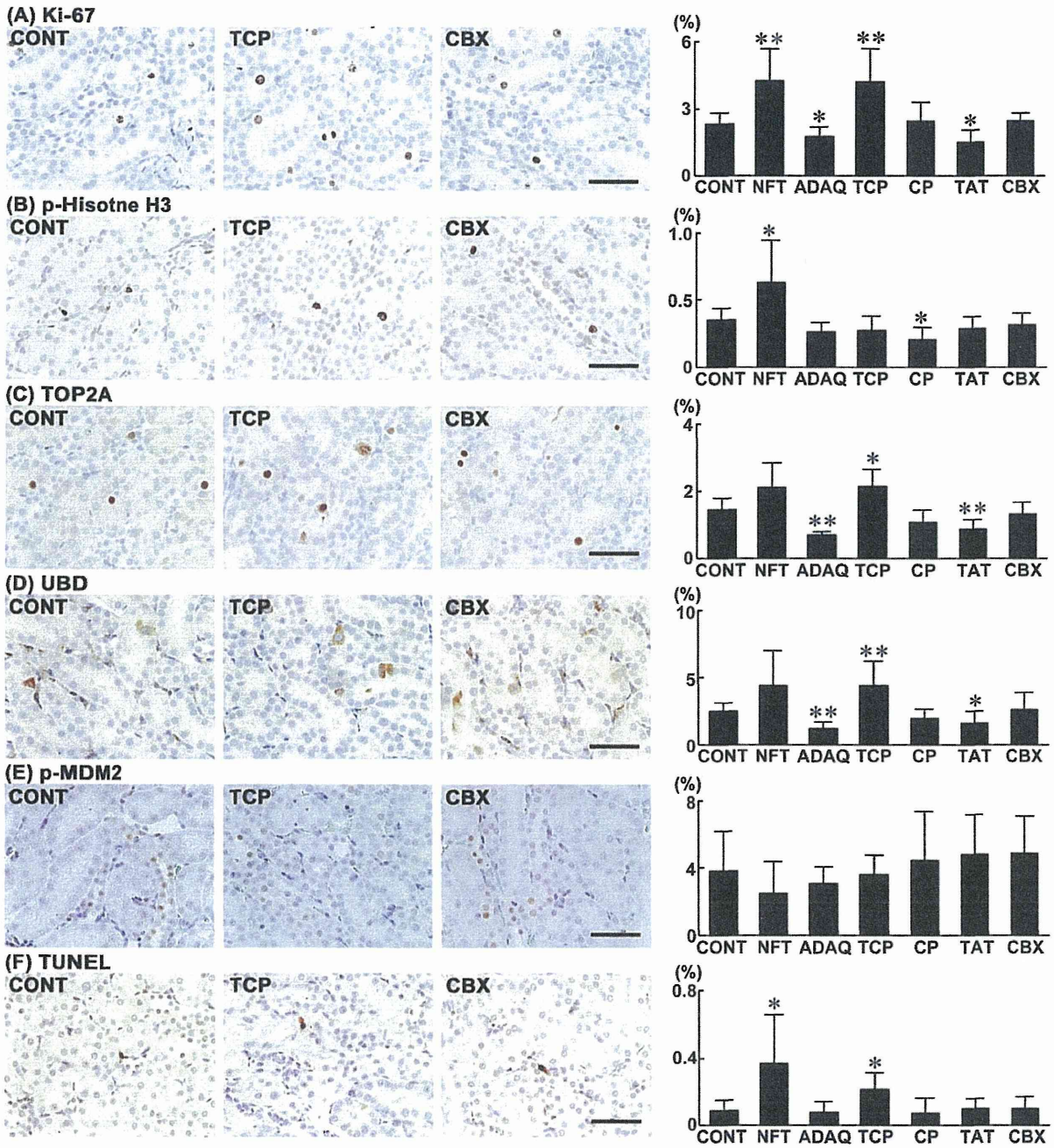

Fig. 13. Distribution of Ki-67$^+$, p-Histone H3$^+$, TOP2A$^+$, UBD$^+$, p-MDM2$^+$, and TUNEL$^+$ cells in the OSOM of rats at day 7 after treatment with renal carcinogens or non-carcinogenic renal toxicants. Photomicrographs show the distribution of Ki-67$^+$, p-Histone H3$^+$, TOP2A$^+$, UBD$^+$, p-MDM2$^+$, and TUNEL$^+$ cells in the OSOM of representative cases from untreated controls and animals treated with TCP or CBX. The graphs show positive cell ratios of renal tubular epithelial cells per total cells counted in 10 animals of each group. Values represent mean + SD. (A) Ki-67, (B) p-Histone H3, (C) TOP2A, (D) UBD, (E) p-MDM2, and (F) TUNEL. Bar = 50 μm. * $P < 0.05$, ** $P < 0.01$ vs. untreated controls (Steel's test).

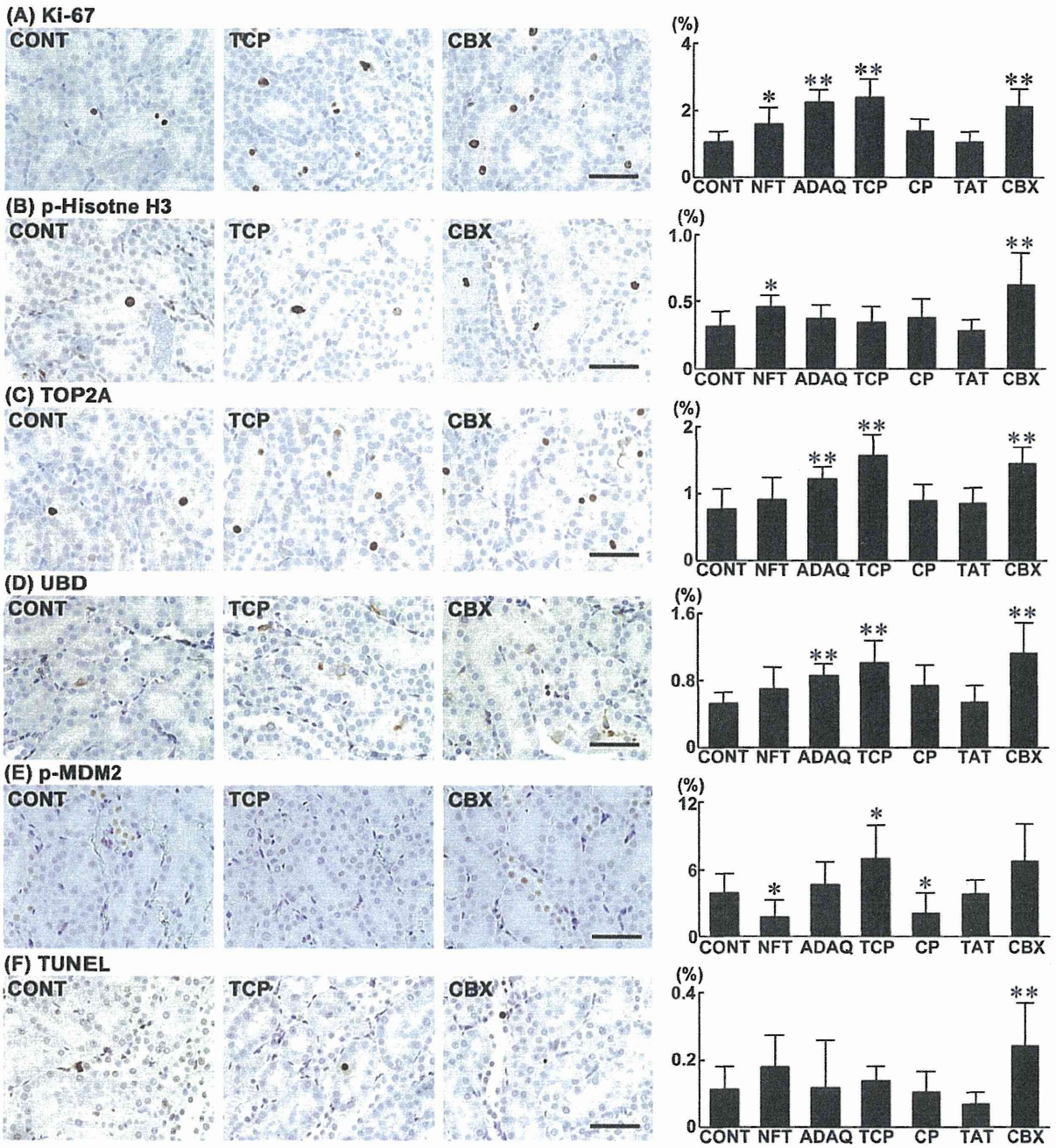

Fig. 14. Distribution of Ki-67$^+$, p-Histone H3$^+$, TOP2A$^+$, UBD$^+$, p-MDM2$^+$, and TUNEL$^+$ cells in the OSOM of rats at day 28 after treatment with renal carcinogens or non-carcinogenic renal toxicants. Photomicrographs show the distribution of Ki-67$^+$, p-Histone H3$^+$, TOP2A$^+$, UBD$^+$, p-MDM2$^+$, and TUNEL$^+$ cells in the OSOM of representative cases from untreated controls and animals treated with TCP or CBX. The graphs show positive cell ratios of renal tubular epithelial cells per total cells counted in 10 animals of each group. Values represent mean + SD. (A) Ki-67, (B) p-Histone H3, (C) TOP2A, (D) UBD, (E) p-MDM2, and (F) TUNEL. Bar = 50 μm. * $P < 0.05$, ** $P < 0.01$ vs. untreated controls (Dunnett's or Steel's test).