## **Supplementary Material**



Time course of circulating osteoprotegerin (OPG) levels during human fracture healing according to age and sex. Time course of OPG is illustrated as mean and standard error of the mean (SEM) according to: a) and b) sex; and c) and d) age. Differences between groups are illustrated in a) and c). For better visualization of time course during fracture healing, groups were adjusted to equal baseline levels, as illustrated in b) and d). In b) and d), significant changes are illustrated according to paired analyses for each group. \*p < 0.05;  $\dagger p < 0.005$ .



Time course of circulating soluble receptor activator of nuclear factor kappa-B (NF-Kb) ligand (sRANKL) levels during human fracture healing according to age and sex. Time course of sRANKL is illustrated as mean and standard error of the mean (sEM), according to: a) and b) sex; and c) and d) age. Differences between groups are illustrated in a) and c). For better visualization of time course during fracture healing, groups were adjusted to equal baseline levels, as illustrated in b) and d). In b) and d), significant changes are illustrated according to paired analyses for each group. \*p < 0.05.



Time course of circulating osteoprotegerin (OPG) levels during human fracture healing according to smoking, alcohol, and diabetes. Time course of OPG is illustrated as mean and standard error of the mean (SEM) according to: a) and b) smoking status; c) and d) alcohol intake; and e) and f) diabetes. Differences between groups are illustrated in a), c), and e). For better visualization of time course during fracture healing, groups were adjusted to equal baseline levels, as illustrated in b), d), and f). In b), d), and f), significant changes are illustrated according to paired analyses for each group. \*p < 0.05.



Time course of circulating soluble receptor activator of nuclear factor kappa-B (NF-Kb) ligand (sRANKL) levels during human fracture healing according to smoking, alcohol and diabetes. Time course of sRANKL is illustrated as mean and standard error of the mean (SEM) according to: a) and b) smoking status; c) and d) alcohol intake; and e) and f) diabetes. Differences between groups are illustrated in a), c) and e). For better visualization of time course during fracture healing, groups were adjusted to equal baseline levels, as illustrated in b), d) and f). In b), d) and f), significant changes are illustrated according to paired analyses for each group. \*p < 0.05.