Legends to supplementary figures

Figure S1: The average number of molecules of PO-PEG-COOH per nanocrystal was measured by Fourier Transform Infrared Spectroscopy. Infrared spectra in KBr pellets of various proportions of PO-PEG-COOH mixed with a constant amount of USPIONs were recorded. The normalized 1110 cm^{-1} band was used for the establishment of the calibration curve and the average number of PO-PEG-COOH per nanoparticle was deduced from this curve and evaluated to 176 ± 16.

Figure S2: Calibration curve using gastrin peptide by OPA assay.

Figure S3: a) CCK2R expression in CAF cell lines. Two immortalized human cancer-associated fibroblasts (CAF) cell lines, CAF1 and CAF2, were permanently transfected with an expression vector encoding the human CCK2R. 2 clones expressing the CCK2R were selected and termed respectively CAF1-CCK2 and CAF2-CCK2. Cells were incubated with 10 nM DY647-CCK9 agonist in presence or in absence of 10 µM GV 150013X, a specific CCK2R antagonist. Cell-associated fluorescence was determined by flow cytometry, revealing the expression of CCK2R on CAF cell lines. b) USPION@Gastrin uptake depends on CCK2R expression. Cells were incubated with increased concentrations of USPION@Gastrin in presence or in absence of 10 µM Gastrin-17, a specific CCK2R agonist, for 24 h. Cell-associated fluorescence was measured by flow cytometry. Results are expressed as fluorescence associated with the cells and are the mean ± SEM of at least three separate experiments.

Figure S4: Analysis of CAFs death upon 40 mT RMF exposure. CAF1-CCK2 cells were incubated for 24 h with increased concentration of USPION@Gastrin (4, 8 and 16 µg magnetic Fe / ml), washed and exposed to RMF for 2 h. Different frequencies (0.2, 1, 10, 20 Hz) were assayed. Dead cells were labeled with AnnV/PI, 4h after RMF exposure, and counted by flow cytometry. Results are expressed as mean ± SEM of at least three separate experiments. Statistical analysis was performed using two-way ANOVA test.

Figure S5: Analysis of CAFs death upon 20 mT RMF exposure. CAF1-CCK2 cells were incubated for 24 h with increased concentration of USPION@Gastrin (4, 8 and 16 µg magnetic Fe / ml), washed and exposed to RMF for 2 h. Different frequencies (1, 10, 20 Hz) were assayed. Dead cells were labeled with AnnV/PI, 4h after RMF exposure, and counted by flow cytometry. Results are expressed as mean ± SEM of at least three separate experiments. Statistical analysis was performed using two-way ANOVA test.

Figure S6: Analysis of CAFs death upon 60 mT / 1 Hz RMF exposure. CAF1-CCK2 cells were incubated for 24 h with increased concentration of USPION@Gastrin (4, 8 and 16 µg magnetic Fe / ml), washed and exposed to RMF for 2 h. Dead cells were labeled with AnnV/PI, 4h after RMF exposure, and counted by flow cytometry. Results are expressed as mean ± SEM of at least three separate experiments. Statistical analysis was performed using two-way ANOVA test.

Figure S7: Analysis of CAFs death upon 200 mT RMF exposure. CAF1-CCK2 cells were incubated for 24 h with increased concentration of USPION@Gastrin (4, 8 and 16 µg magnetic Fe

/ ml), washed and exposed to RMF for 2 h. Different frequencies (1, 10, 20 Hz) were assayed. Dead cells were labeled with AnnV/PI, 4h after RMF exposure, and counted by flow cytometry. Results are expressed as mean ± SEM of at least three separate experiments. Statistical analysis was performed using two-way ANOVA test.

Figure S8: Analysis of CAFs death upon 380 mT RMF exposure. CAF1-CCK2 cells were incubated for 24 h with increased concentration of USPION@Gastrin (4, 8 and 16 µg magnetic Fe / ml), washed and exposed to RMF for 2 h. Different frequencies (1, 10, 20 Hz) were assayed. Dead cells were labeled with AnnV/PI, 4h after RMF exposure, and counted by flow cytometry. Results are expressed as mean ± SEM of at least three separate experiments. Statistical analysis was performed using two-way ANOVA test.

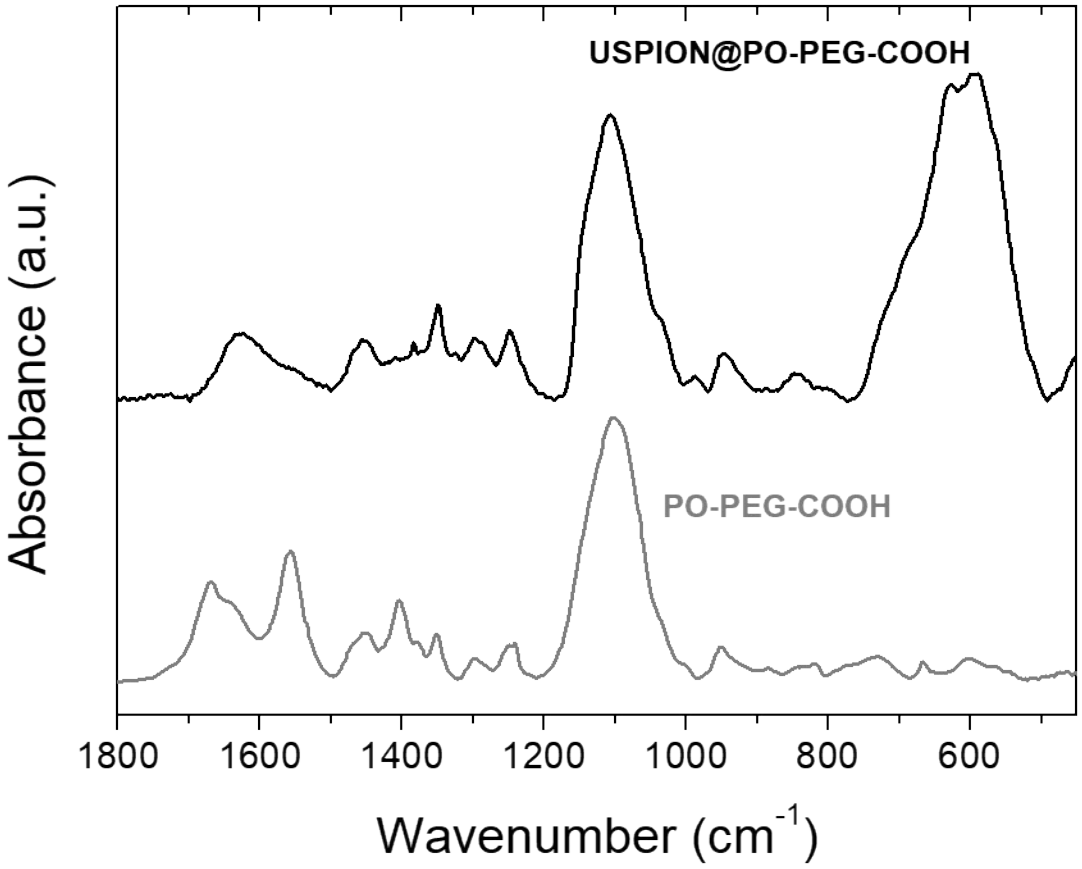

USPION@PO-PEG-COOH
PO-PEG-COOH
Absorbance (a.u.)
1800
1600
1400
1200
1000
800
600
Wavenumber (cm-1)

Figure S1

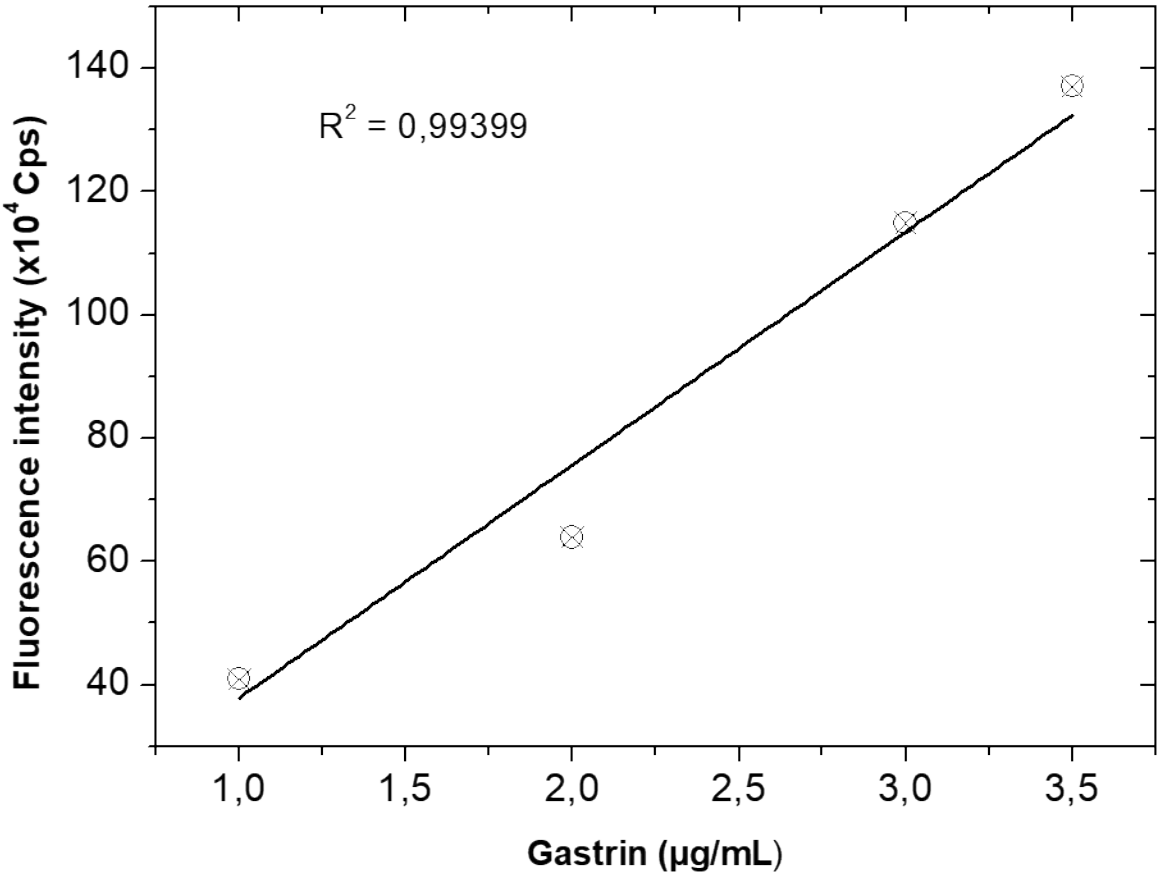
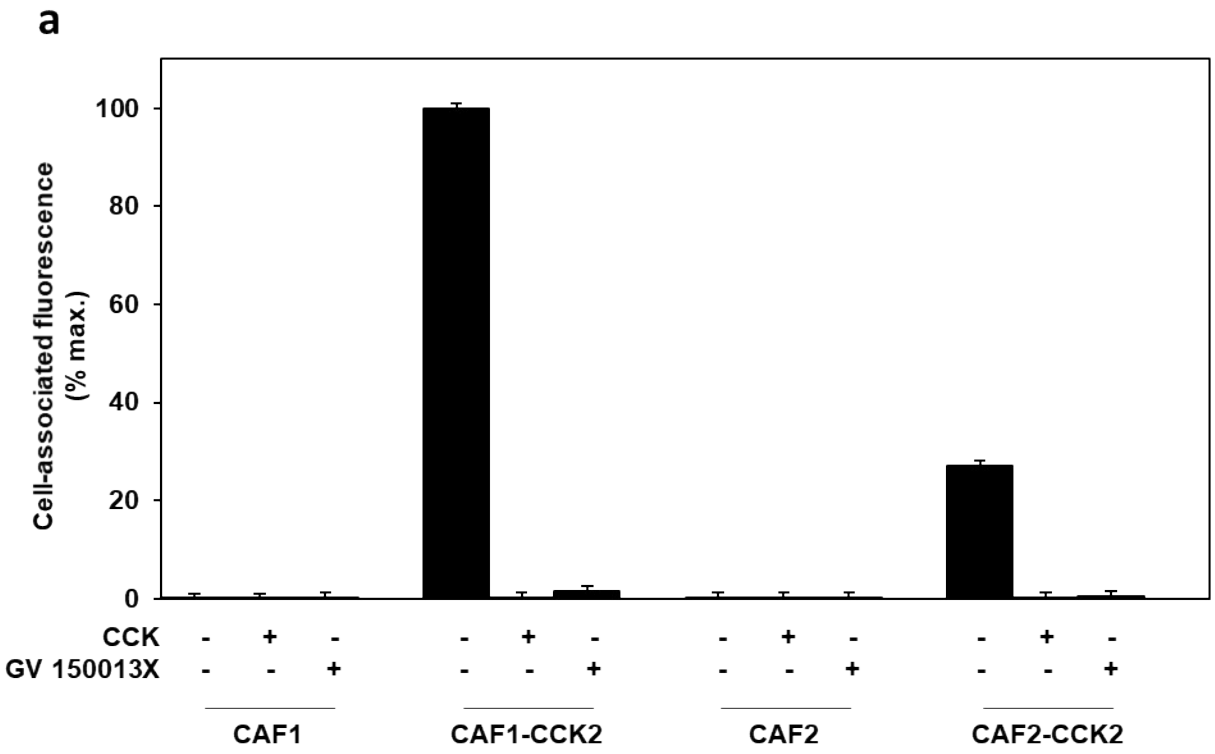

Fluorescence intensity (x10^4 Cps)
140
120
100
80
60
40
R^2 = 0,99399
1,0
1,5
2,0
2,5
3,0
3,5
Gastrin (µg/mL)

Figure S2


a
Cell-associated fluorescence (% max.)
100
80
60
40
20
0
CCK - + - - + - - + - - + -
GV 150013X - - + - - + - - + - - +
CAF1
CAF1-CCK2
CAF2
CAF2-CCK2

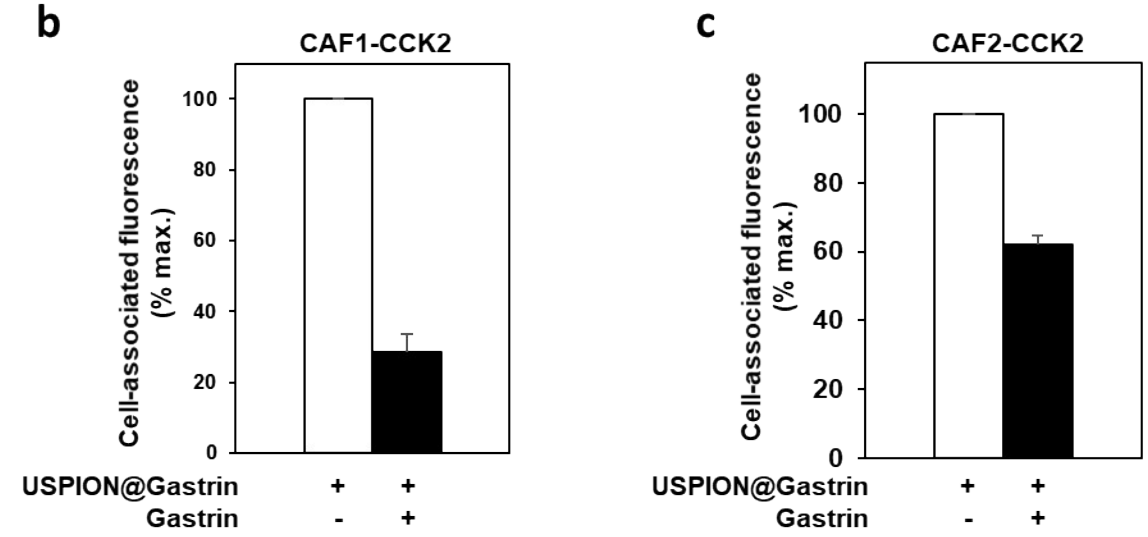

b
CAF1-CCK2
Cell-associated fluorescence (% max.)
100
80
60
40
20
0
USPION@Gastrin + +
Gastrin - +
c
CAF2-CCK2
Cell-associated fluorescence (% max.)
100
80
60
40
20
0
USPION@Gastrin + +
Gastrin - +

Figure S3

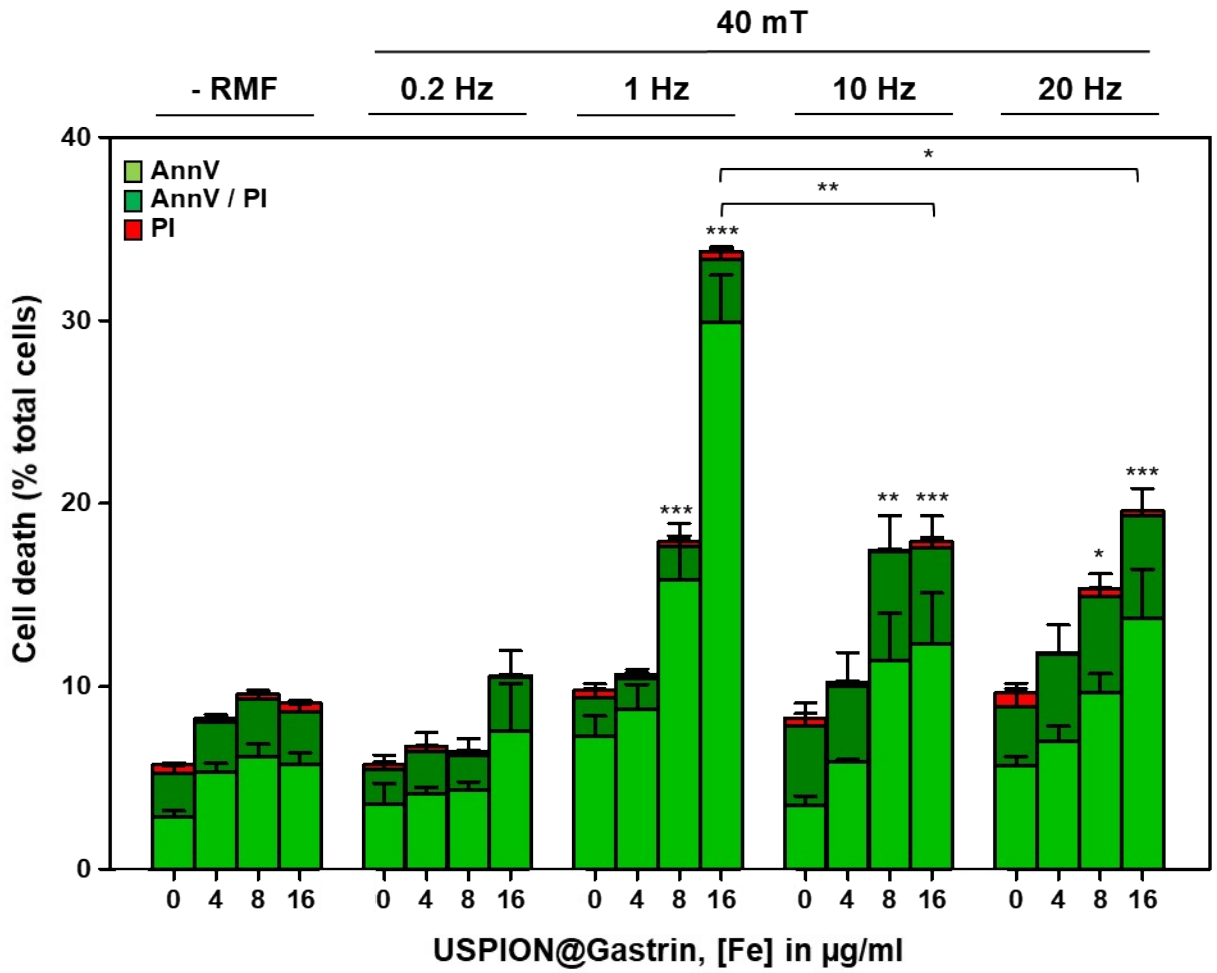

40 mT
- RMF
0.2 Hz
1 Hz
10 Hz
20 Hz
AnnV
AnnV / PI
PI
Cell death (% total cells)
USPION@Gastrin, [Fe] in µg/ml
0
4
8
16
10
20
30
40
*
**
***

Figure S4

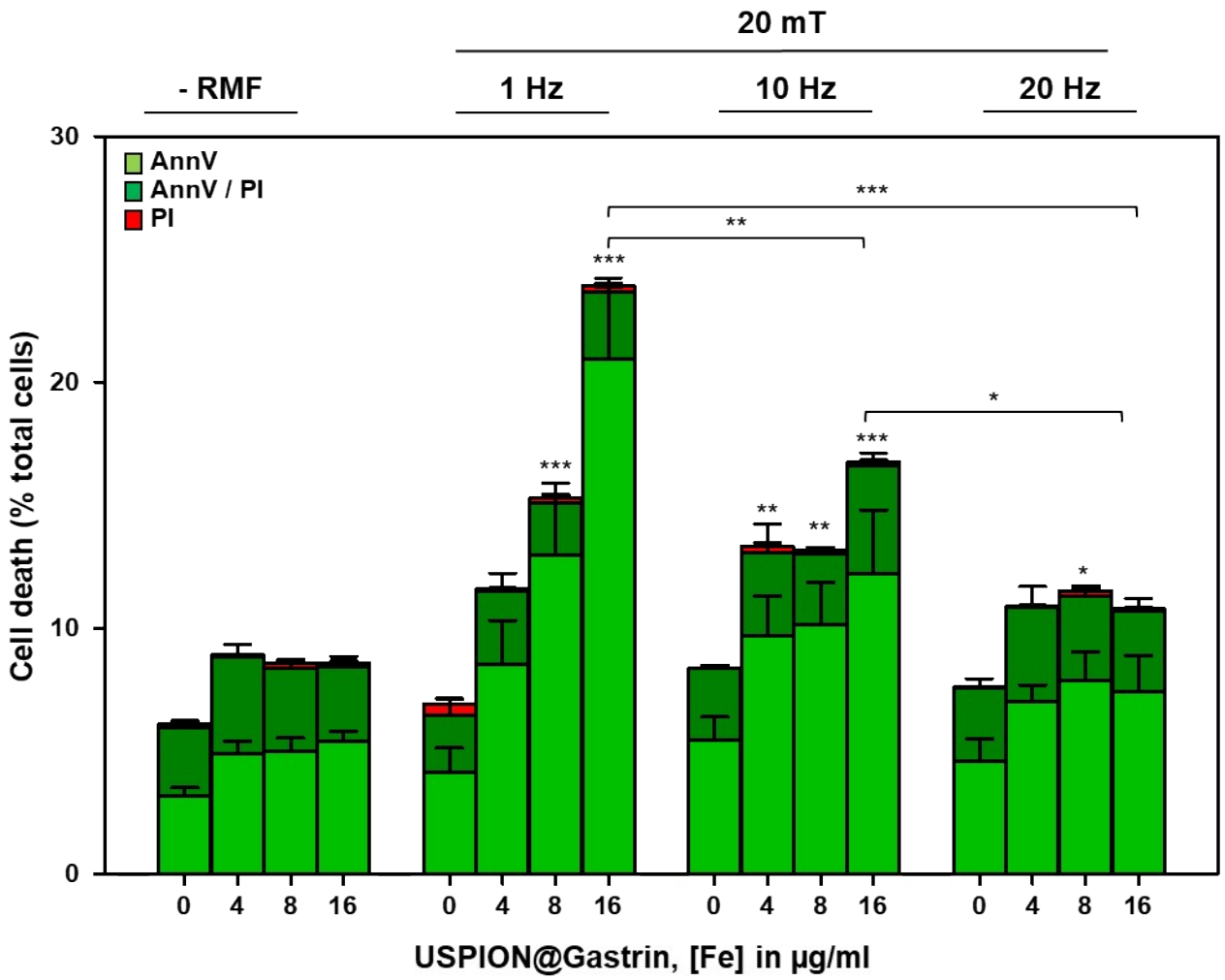

20 mT
- RMF
1 Hz
10 Hz
20 Hz
AnnV
AnnV / PI
PI
Cell death (% total cells)
30
20
10
0
***
**
***
***
**
**
***
*
*
0
4
8
16
USPION@Gastrin, [Fe] in µg/ml

Figure S5

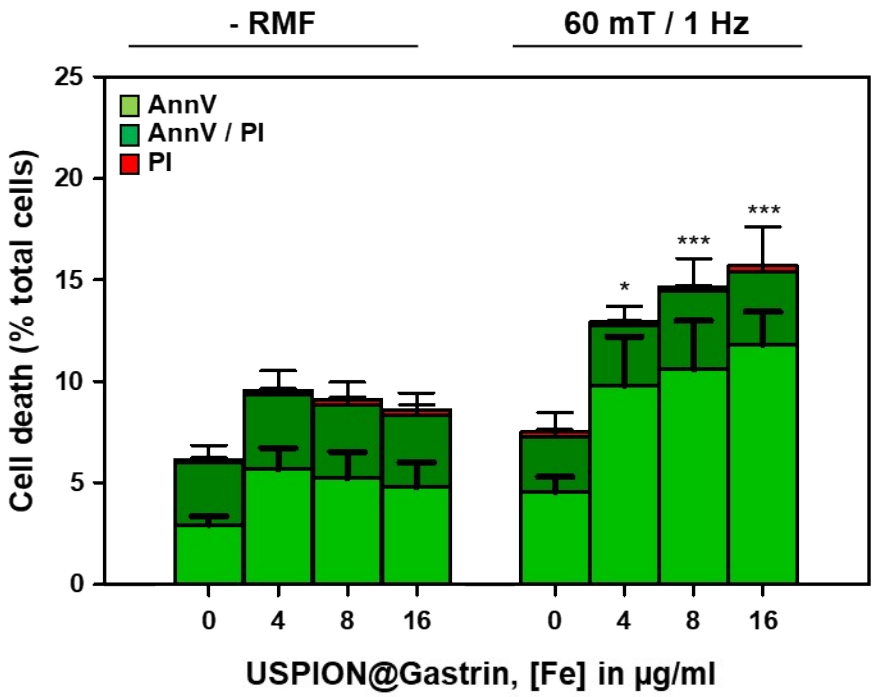

- RMF
60 mT / 1 Hz
AnnV
AnnV / PI
PI
Cell death (% total cells)
25
20
15
10
5
0
*
***
***
0
4
8
16
0
4
8
16
USPION@Gastrin, [Fe] in µg/ml

Figure S6

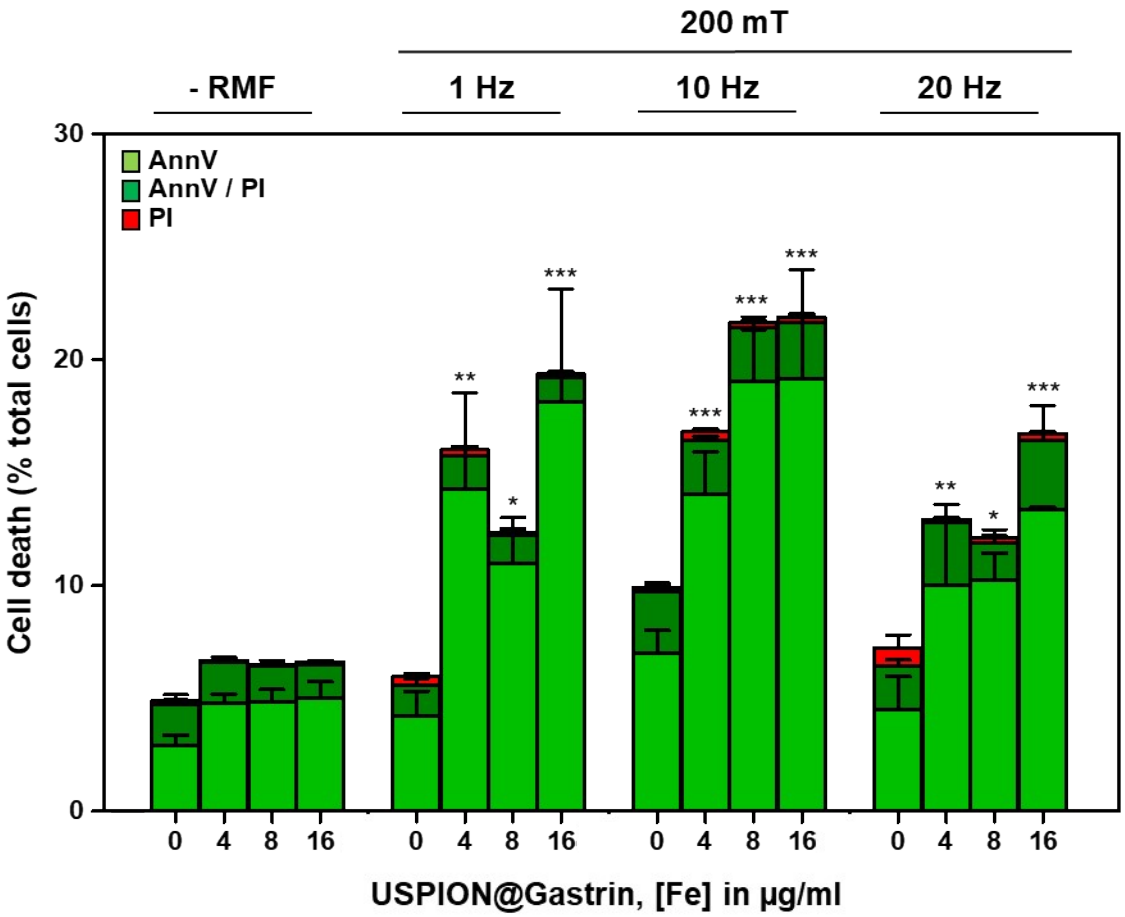

200 mT
- RMF
1 Hz
10 Hz
20 Hz
AnnV
AnnV / PI
PI
Cell death (% total cells)
30
20
10
0
0 4 8 16 0 4 8 16 0 4 8 16 0 4 8 16
USPIO@Gastrin, [Fe] in µg/ml

Figure S7

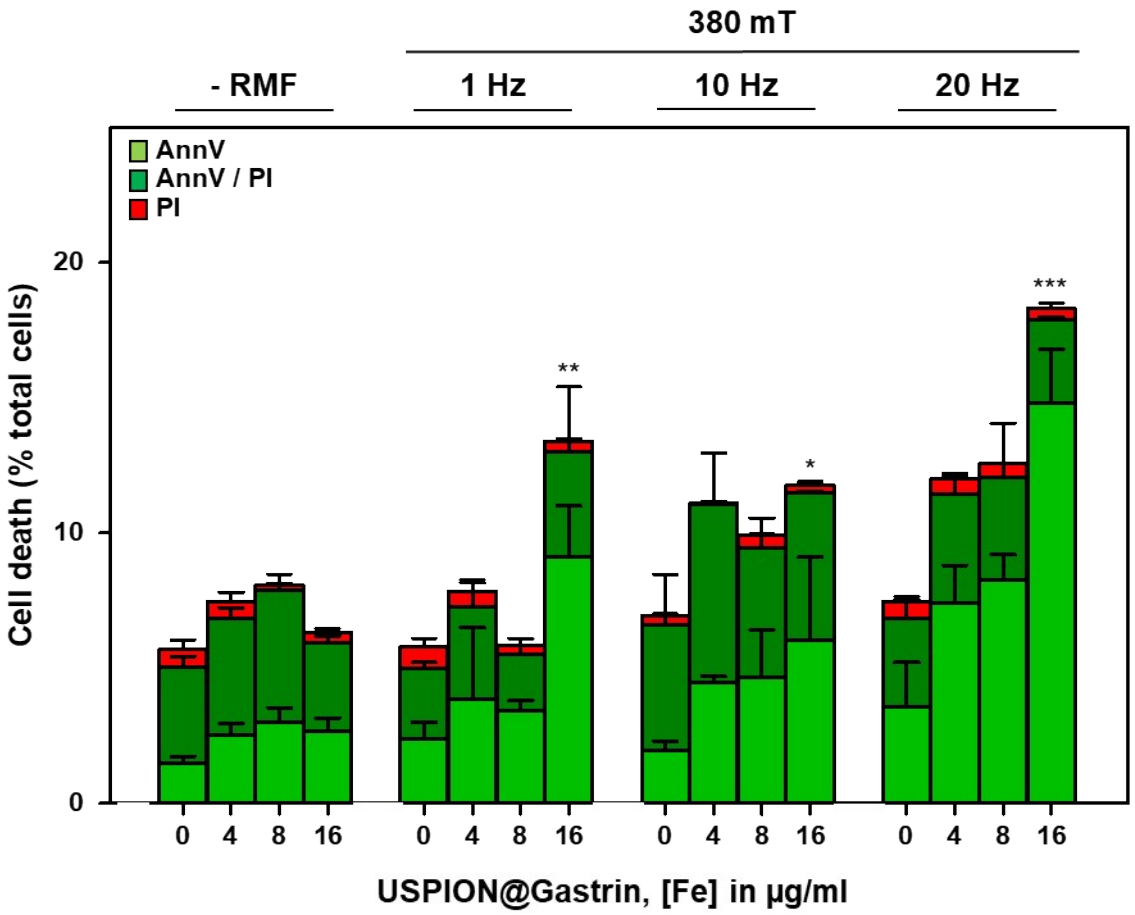

380 mT
- RMF
1 Hz
10 Hz
20 Hz
AnnV
AnnV / PI
PI
Cell death (% total cells)
0
10
20
**
*
***
0 4 8 16 0 4 8 16 0 4 8 16 0 4 8 16
USPION@Gastrin, [Fe] in µg/ml

Figure S8