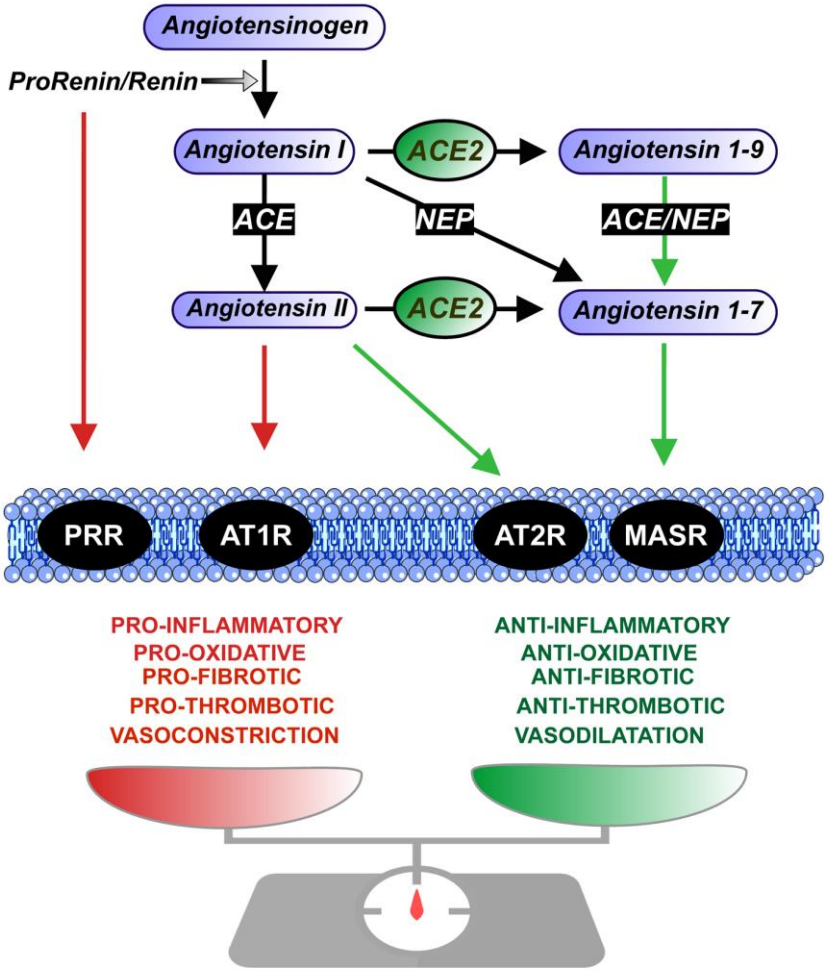
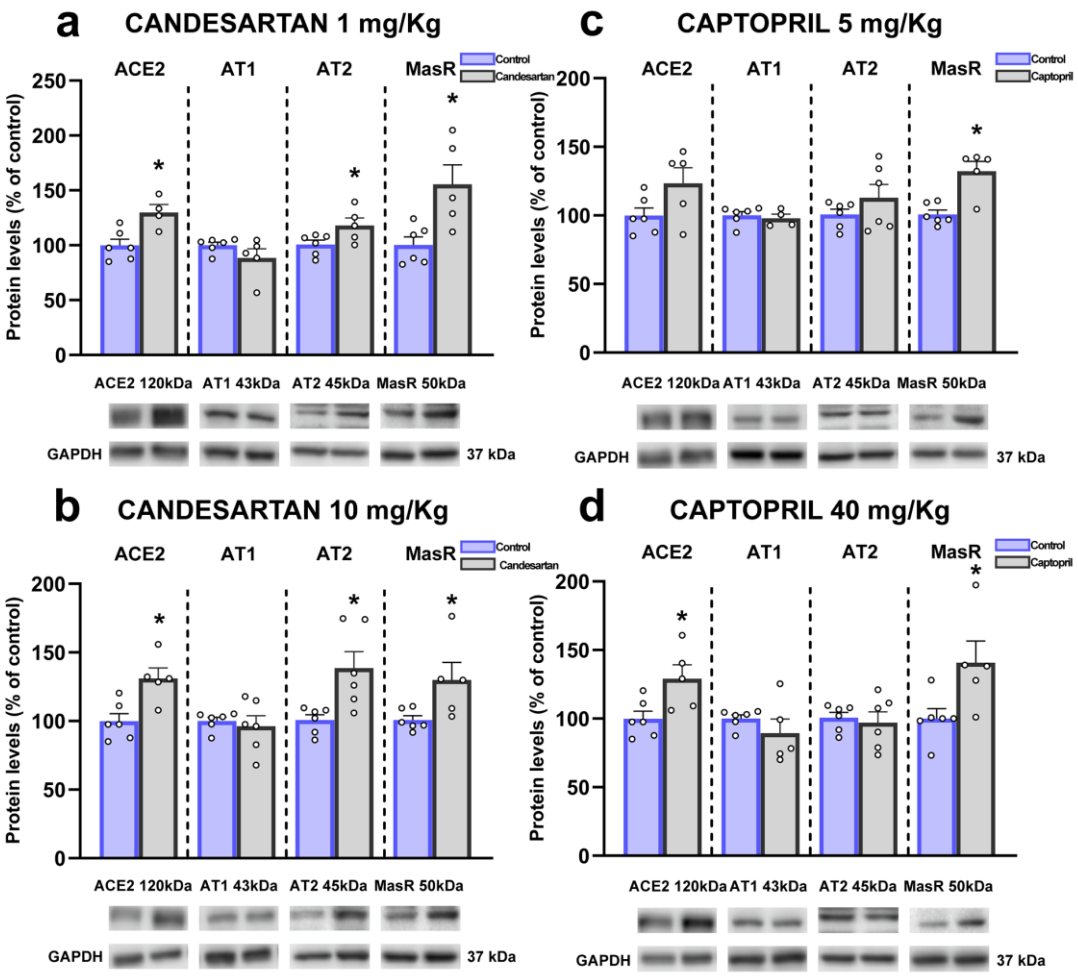
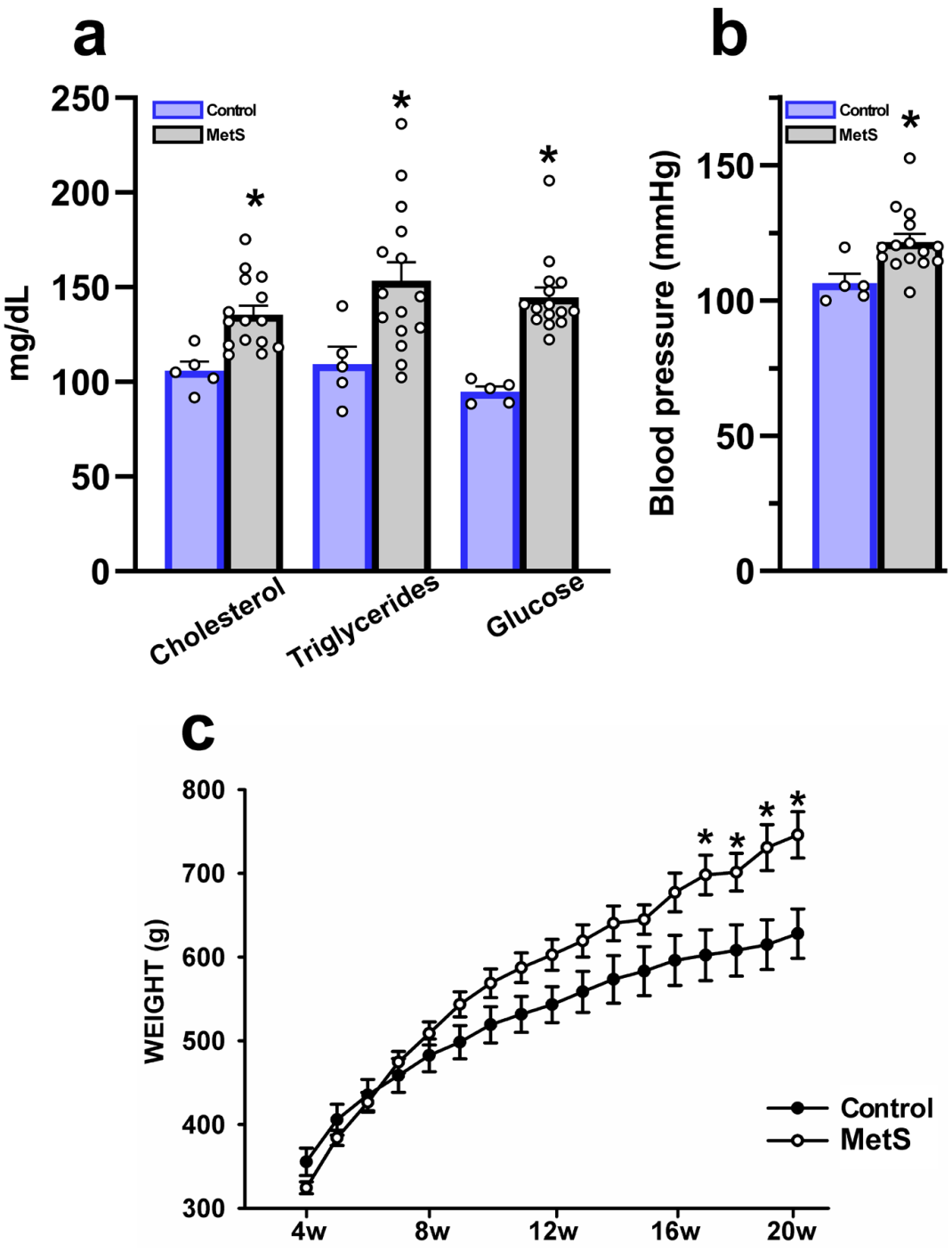

Angiotensinogen
ProRenin/Renin
Angiotensin I
ACE2
Angiotensin 1-9
ACE
NEP
ACE/NEP
Angiotensin II
ACE2
Angiotensin 1-7
PRR
AT1R
AT2R
MASR
PRO-INFLAMMATORY
PRO-OXIDATIVE
PRO-FIBROTIC
PRO-THROMBOTIC
VASOCONSTRICTION
ANTI-INFLAMMATORY
ANTI-OXIDATIVE
ANTI-FIBROTIC
ANTI-THROMBOTIC
VASODILATATION

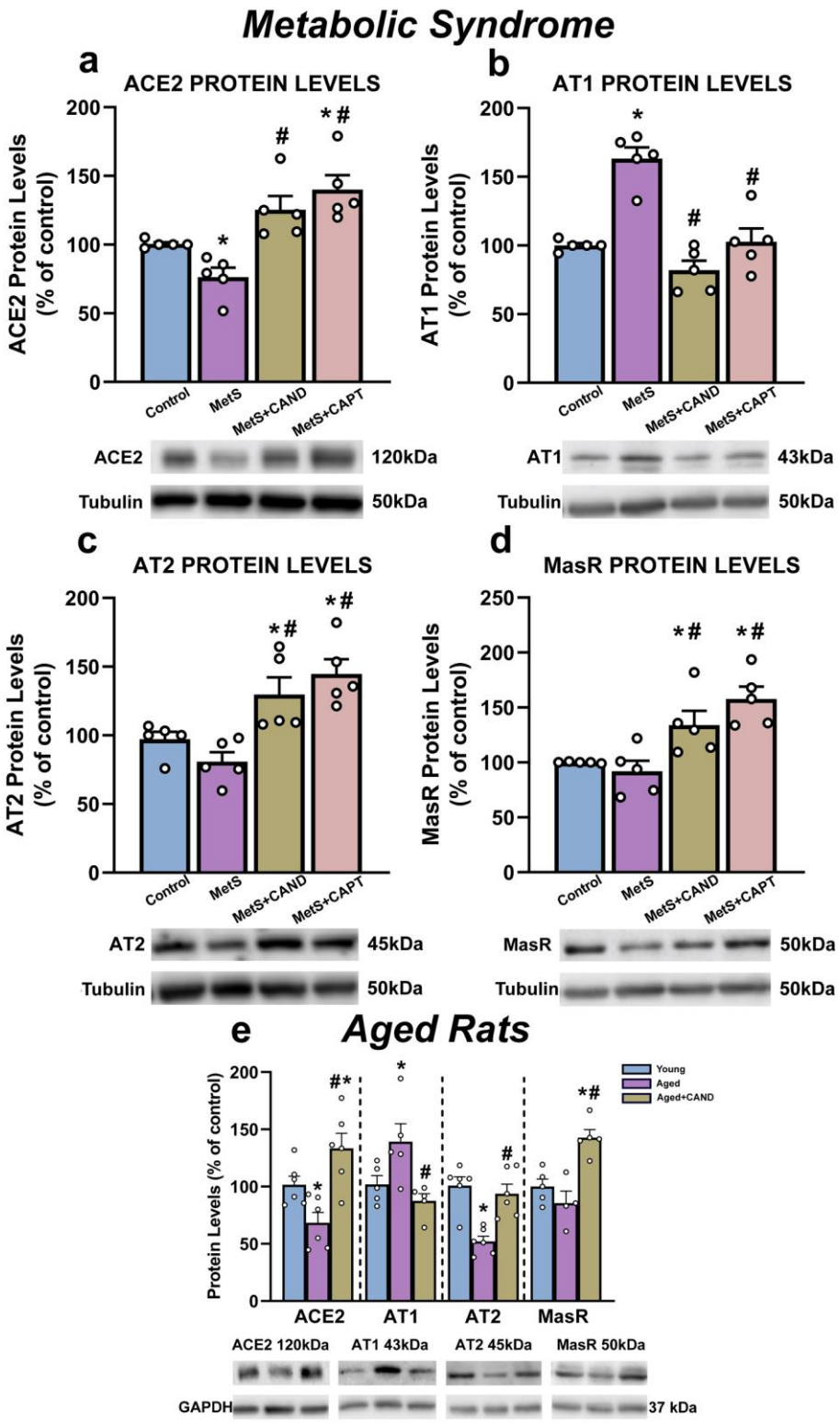
Supplementary Figure 1. The renin–angiotensin system (RAS) is basically organized into two arms that counteract each other: a pro-inflammatory and pro-oxidative axis (red lines) mainly formed by angiotensin II and AT1 receptors (AT1R), and an anti-inflammatory anti-oxidative axis (green lines) formed by Angiotensin II/AT2R, and particularly Angiotensin 1-7 /MasR. Angiotensin II is formed by the sequential action of two enzymes prorenin/renin (that forms angiotensin I) and angiotensin converting enzyme (ACE) on the precursor protein angiotensinogen. Renin and its precursor prorenin (PR) also act on specific PR receptors. Angiotensin converting enzyme 2 (ACE2) plays a key role in the balance, because ACE2 (together with additional peptidases such as Neprilysin, NE) transforms components of the pro-inflammatory axis (i.e. Angiotensin I and particularly Angiotensin II) into components of the anti-inflammatory axis (i.e. Angiotensin 1-9, and particularly Angiotensin 1-7).


a
CANDESARTAN 1 mg/Kg
Control
Candesartan
ACE2
AT1
AT2
MasR
Protein levels (% of control)
250
200
150
100
50
0
*
ACE2 120kDa
AT1 43kDa
AT2 45kDa
MasR 50kDa
GAPDH
37 kDa
c
CAPTOPRIL 5 mg/Kg
Control
Captopril
ACE2
AT1
AT2
MasR
Protein levels (% of control)
200
150
100
50
0
*
ACE2 120kDa
AT1 43kDa
AT2 45kDa
MasR 50kDa
GAPDH
37 kDa
b
CANDESARTAN 10 mg/Kg
Control
Candesartan
ACE2
AT1
AT2
MasR
Protein levels (% of control)
200
150
100
50
0
*
ACE2 120kDa
AT1 43kDa
AT2 45kDa
MasR 50kDa
GAPDH
37 kDa
d
CAPTOPRIL 40 mg/Kg
Control
Captopril
ACE2
AT1
AT2
MasR
Protein levels (% of control)
200
150
100
50
0
*
ACE2 120kDa
AT1 43kDa
AT2 45kDa
MasR 50kDa
GAPDH
37 kDa

Supplementary Figure 2. Effects of candesartan (**a, b**) and captopril (**c, d**) on protein expression of ACE2 and AT1, AT2 and Mas receptors in the adult rat lung. Data are mean ± SEMs. *$p<0.05$ relative to control group(Student´s test and Mann-Whitney Rank Sum Test)


a
b
c
Control
MetS
mg/dL
250
200
150
100
50
0
Cholesterol
Triglycerides
Glucose
Blood pressure (mmHg)
150
100
50
0
WEIGHT (g)
800
700
600
500
400
300
4w
8w
12w
16w
20w
*

Supplementary Figure 3. Rats with metabolic syndrome (MetS) showed a significant increase in blood levels of cholesterol, triglycerides and glucose (**a**), significant increase in blood pressure (**b**) and increase in weight relative to control rats (**c**) (Student´s test and Mann-Whitney Rank Sum Test).


Metabolic Syndrome
a
ACE2 PROTEIN LEVELS
ACE2 Protein Levels (% of control)
Control
MetS
MetS+CAND
MetS+CAPT
ACE2
120kDa
Tubulin
50kDa
b
AT1 PROTEIN LEVELS
AT1 Protein Levels (% of control)
AT1
43kDa
c
AT2 PROTEIN LEVELS
AT2 Protein Levels (% of control)
AT2
45kDa
d
MasR PROTEIN LEVELS
MasR Protein Levels (% of control)
MasR
50kDa
e
Aged Rats
Young
Aged
Aged+CAND
Protein Levels (% of control)
ACE2
AT1
AT2
MasR
ACE2 120kDa
AT1 43kDa
AT2 45kDa
MasR 50kDa
GAPDH
37 kDa

Supplementary Figure 4. Protein levels of ACE2 (**a**) and AT1 (**b**), AT2 (**c**) and Mas (**d**) receptors in the lung of control rats and rats with metabolic syndrome (MetS) untreated or treated with candesartan and captopril, and aged rats untreated or treated with candesartan (**e**). Data are mean ± SEMs. *$p<0.05$ relative to control adult rats, #$p<0.05$ relative to untreated rats with metabolic syndrome (**a-d**) or aged rats (**e**). (one-way ANOVA with Student-Newman-Keuls Method post hoc test or Kruskal-Wallis One Way Analysis of Variance on Ranks with Student-Newman-Keuls Method post hoc test). CAND, Candesartan; CAPT, Captopril.