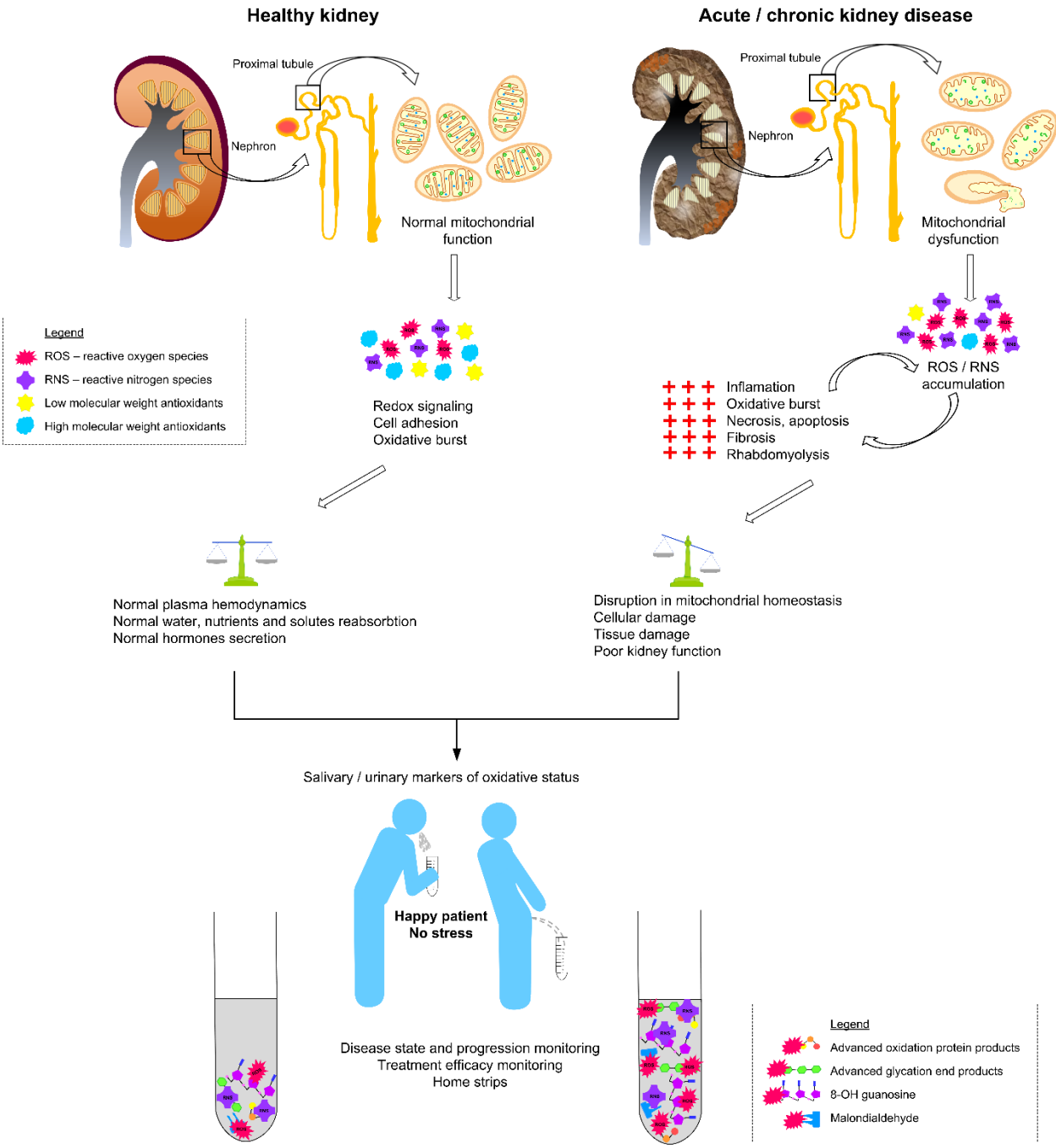Graphical Abstract