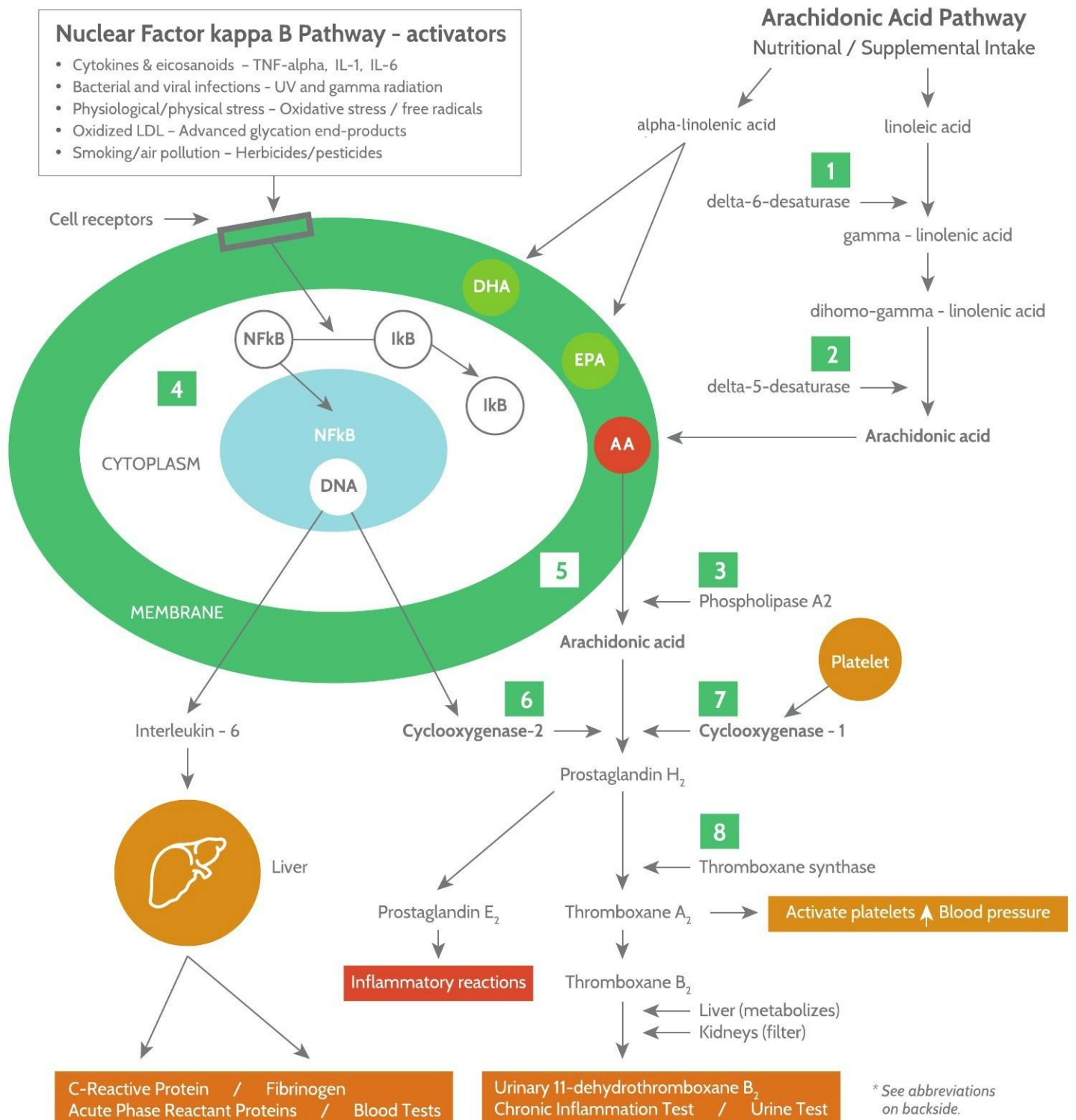


## CHRONIC INFLAMMATION PATHWAY

### Relationship Between Biomarkers of Inflammation



# MECHANISMS OF THROMBOXANE A<sub>2</sub> GENERATION AND REGULATION

## Major Sites of Physiologic Intervention

SITE	PHYSIOLOGIC ACTION
1	delta-6-desaturase; up-regulation increases AA – down-regulation decreases AA production.
2	delta-5-desaturase; up-regulation increases AA – down-regulation decreases AA production.
3	Phospholipase A2; regulates the liberation of fatty acids (AA,EPA,DHA) from cell membrane phospholipids.
4	Nuclear Factor kappa B; in cell nucleus, activates genes (cyclooxygenase – 2, interleukin – 6 and others).
5	Cell membrane fatty acids; AA/EPA ratio increased – (inflammatory); AA/EPA ratio decreased – (anti-inflammatory).
6	Cyclooxygenase – 2; catalyzes formation of prostaglandins and thromboxanes.
7	Cyclooxygenase – 1; catalyzes formation of prostaglandins and thromboxanes.
8	Thromboxane synthase; catalyzes metabolic synthesis producing thromboxane A <sub>2</sub> .

## EXAMPLES OF CHRONIC INFLAMMATION INTERVENTIONAL THERAPY

THERAPY	SITE	MECHANISM OF PHYSIOLOGICAL ACTION
Aspirin	7	Inhibits COX – 1 in low dosages (81,162, & 325 mg/day), reducing thromboxane A <sub>2</sub> .
	6	Inhibits COX – 2 in higher dosages (325 mg/day +). Reducing thromboxane A <sub>2</sub> .
	4	Inhibits activation of NFk B, reducing COX-2 availability.
Corticosteroids, cortisol & synthetic derivatives	3	Inhibits Phospholipase A2, reducing AA availability.
	4	Inhibits activation of NFkB, reducing COX-2 availability.
Exercise - regular aerobic - intense	4	Inhibits activation of NFkB, reducing COX-2 availability.
	4	Increases activation of NFkB, increasing COX-2 availability.
Meditation	6	Decreases expression of COX – 2 gene, reducing COX-2 availability.
Omega-3 / fatty acids	2	Down-regulates delta-5 desaturase, reducing AA production.
	3	Inhibits Phospholipase A2 activity reducing AA availability.
	5	EPA and DHA compete with AA in cell membranes, reducing AA availability.
	4	Inhibits NFkB activity, reducing cyclooxygenase-2 availability.
Phytonutrients <b>Carotenoids, flavonoids, polyphenols</b> (fruits & vegetables, tea, wine, chocolate, olive oil, herbs & spices, nuts & seeds, curcumin, quercetin)	4	Inhibits activation of Nuclear Factor kappa B, reducing COX-2 availability.
Smoking cessation	4	Reduces activation of NFkB, reducing COX-2 availability.
	8	Reduces thromboxane synthase activity, reducing TXA <sub>2</sub> levels.
Vitamin E	3	Inhibits Phospholipase A2 activity, reducing AA availability.

### ABBREVIATIONS

AA	Arachidonic Acid	DHA	Docosahexaenoic acid	NFkB	Nuclear Factor kappa B
COX	Cyclooxygenase	EPA	Eicosapentaenoic acid		