

**[P-15]****INHIBITION OF LPS-INDUCED p38 ACTIVATION AND iNOS  
EXPRESSION BY 2-AMINO-3-METHYLIMIDAZO  
[4,5-f]QUINOLINE**Young Jin Jeon

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2-amino-3-methylimidazo[4,5-f]quinoline (IQ), a heterocyclic amine, significantly inhibits nitric oxide (NO) production in lipopolysaccharide (LPS)-stimulated macrophages. The decrease in NO production was found to correlate well with a decrease in iNOS mRNA expression as demonstrated by Northern blot analysis. Treatment of RAW 264.7 cells with IQ selectively inhibited the activation of NF- $\kappa$  B/Rel, an important transcription factor of iNOS gene expression, while neither AP-1 nor Oct was affected by IQ. Since iNOS transcription has been shown recently to be under the control of the p38 kinase signaling cascade, we assessed the effect of IQ on p38 kinase activation. Treatment of RAW 264.7 with IQ inhibited LPS-stimulated p38 kinase phosphorylation in a dose-related manner. IQ also inhibited the p38 kinase activity. Collectively, this series of experiments indicates that IQ inhibits LPS-induced expression of iNOS gene in RAW 264.7 cells. Based on our findings, the most likely mechanism that can account for this biological effect involves the negative regulation of NF- $\kappa$  B/Rel and p38 kinase pathway.

keyword : heterocyclic amine, iNOS, NF- $\kappa$  B/Rel, p38