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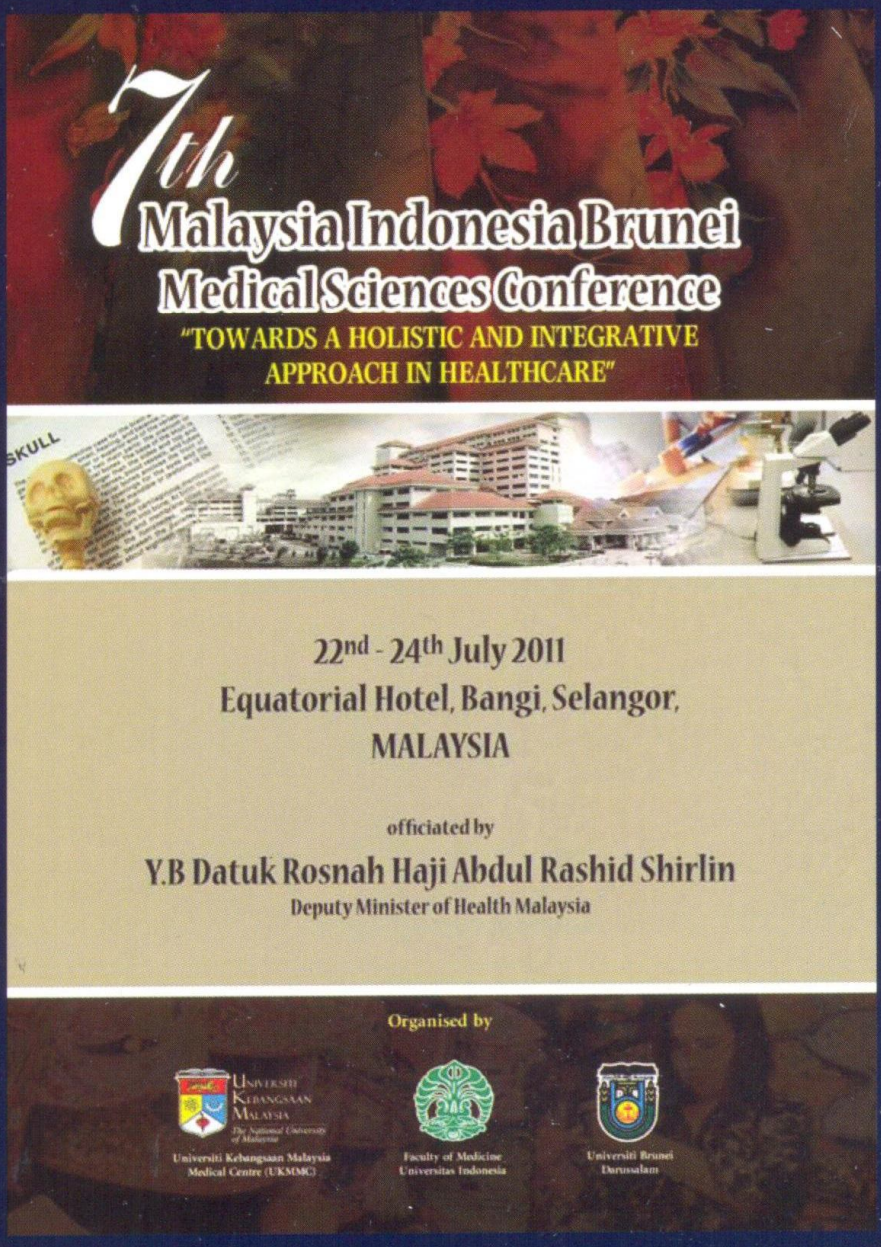

INVOLVEMENT OF $p16^{INK4a}$ IN SENESCENT FIBROBLAST MORPHOGENESIS

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Background:
During cellular senescence, normal human diploid fibroblasts (HDFs) change their morphology from spindle shape to enlarged, flattened and irregular shape. Besides, senescent HDFs express elevated levels of $p16^{INK4a}$ which is known as cyclin-dependent kinase inhibitor (CDKI). The aim of this study was to determine the involvement of $p16^{INK4a}$ in HDFs senescent morphogenesis.

Materials and Methods:
Serial passaging was done and the number of population doublings (PDs) was monitored until HDFs reached senescence (passage 30). Senescent cells were transfected with $p16^{INK4a}$ siRNA for 48 hour and subsequently the RNA was extracted for real time RT PCR analysis.

Results:
Our results showed normal human diploid fibroblasts enter senescence state after 50-60 population doublings. Senescent HDFs showed morphological changes with the presence of senescence-associated β-galactosidase and increased $p16^{INK4a}$ expression. However, senescent HDFs transfected with $p16^{INK4a}$ siRNA showed downregulation of $p16^{INK4a}$ and changes of morphology from senescent morphology to morphology of young cells with the presence of small and spindle shaped fibroblasts.

Conclusion:
In conclusion, increased of $p16^{INK4a}$ expression is correlated with senescent morphology. However, inhibition of $p16^{INK4a}$ expression may delay the onset of cellular senescence.

Keywords:
siRNA, cellular senescence, $p16^{INK4a}$