Hypoxia does not induce degradation of Cx43, PKC-γ or PKC-ε

PKC-ε Knockout Mouse Lenses Show
Abnormal Morphology

Figure 8 - Cytoskeletal images of immunostained Cx43 (Green), PKC-γ and PKC-ε (Red). Typical punctate patterns of junctional Cx43 plaques can be seen in control cells. PKC-γ activators such as TPA, IGF-I and Oxidation (H₂O₂) induce disorganization of the junctional Cx43 and translocation of PKC-γ, but not PKC-ε, to the membrane. FGF-2 does not have any effect on Cx43 plaques and PKC-ε (12 hours) does not affect junctional localization and number of Cx43 plaques as well as the localization of PKC-γ and -ε.

Figure 9 - The number of junctional Cx43 plaques per cell is in normoxic (Control) and hypoxic (5% O₂, 5% CO₂, 37°C, 12 hours) conditions. Hypoxia does not induce degradation of Cx43 junctional plaques.

Summary

1. Stress factors such as phorbol ester (TPA), oxidation (H₂O₂) and IGF-I have opposite effects on enzyme activity in the lens epithelial cells (Figure 2).
2. PKC-γ was activated and PKC-ε was inhibited by phorbol ester (TPA), oxidation, and IGF-I (Figure 2).
3. PKC-ε activators (Figure 3).
4. Phorbol ester (TPA) induces a decreased association of Cx43 with PKC-ε and increased association of PKC-γ with Cx43 (Figure 4).
5. Cx43 colocalizes with PKC-ε (Figure 5).
6. Stress factors such as phorbol ester (TPA), oxidation (H₂O₂) but not hypoxia cause the disassembly of junctional Cx43 plaques (Figure 5).
7. PKC-ε activation by Hypoxia (Figure 3) does not induce the phosphorylation of Cx43 (Figure 6).
8. PKC-γ activation by phorbol ester (TPA), oxidation (H₂O₂) or growth factor (FGF-2) induces the phosphorylation of Cx43 and protein phosphatases of Cx43 (Figure 7).
9. Hypoxia does not induce the disassembly of junctional Cx43 plaques (Figure 8 and 9).
10. Lenses from PKC-ε knockout mice are smaller and have an elongated shape and exhibit abnormal morphology of the bow region (Figure 10).

Conclusion

PKC-γ and PKC-ε have opposing effects on lens Cx43. PKC-γ is activated by stress factors or growth factors and this increases its phosphorylation with Cx43 and displaces PKC-ε from Cx43. Similar treatments cause inhibition of PKC-ε activity and a decreased association of PKC-ε with Cx43. On the contrary, hypoxia, another stress factor, does not affect PKC-γ activity but activates PKC-ε. Results of PKC-ε knockouts mouse lenses suggest that PKC-ε is required for normal lens development.

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