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THE ROLE OF INNATE IMMUNITY AND TUMOR IMMUNE MICROENVIRONMENT (TIME) IN ORAL POTENTIALLY MALIGNANT DISEASE (OPMD) AND RELATED ORAL SQUAMOUS CELL CARCINOMA (OSCC).

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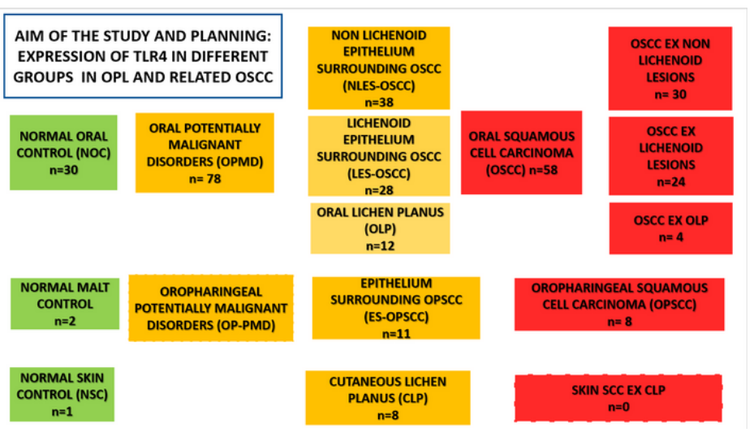
OBJECTIVES



Toll Like Receptors (TLRs) regulate innate and adaptive immune responses. Moreover, TLRs can induce a pro-survival and pro-proliferationresponse in tumorcells. This study aims to investigate the expression of TLR4 in the OralPotentiallyMalignant Disease (OPMD) and related OSCC

METHODS

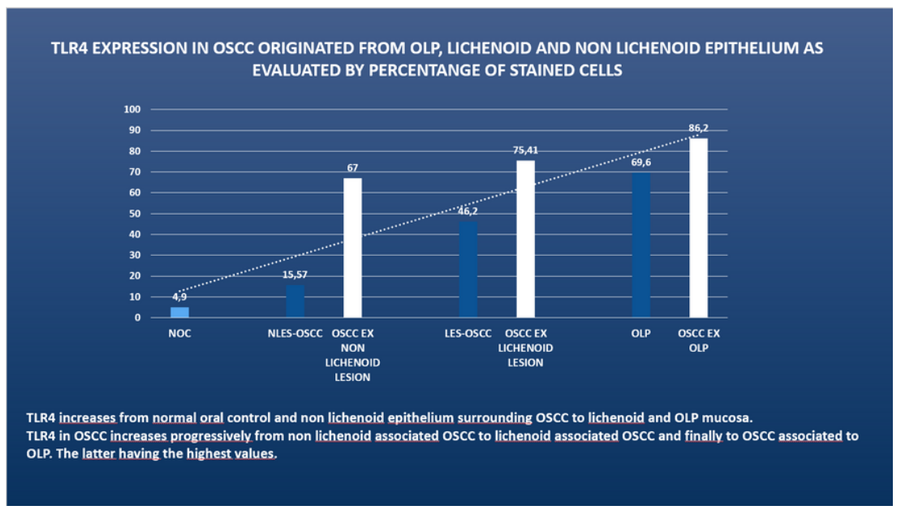
Expression of TLR4 wasdetermined in Oral Lichen Planus (OLP), OralLichenoidLesions (OLL), and related OSCC by standard LSAB-HRP.

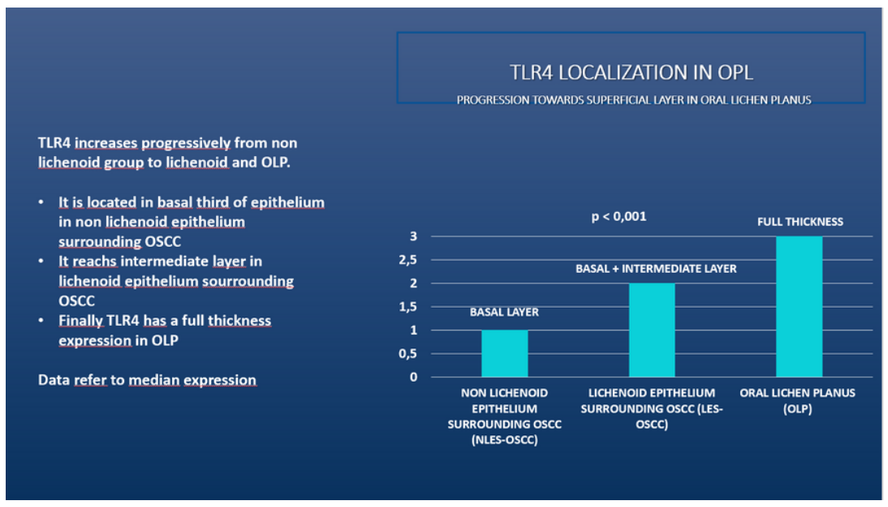
- Immunohistochemistry has been performed with automated LSAB-HRP technique using specific Ab detecting TLR-4.
- Formalin-fixed paraffin embedded tissue
- Immunostained slides were acquired by digital camera and analyzed by ISE TMA Software (Integrated System Engineering, Milan, Italy), and *CellSens V1.9® Olympus image analysis software.*

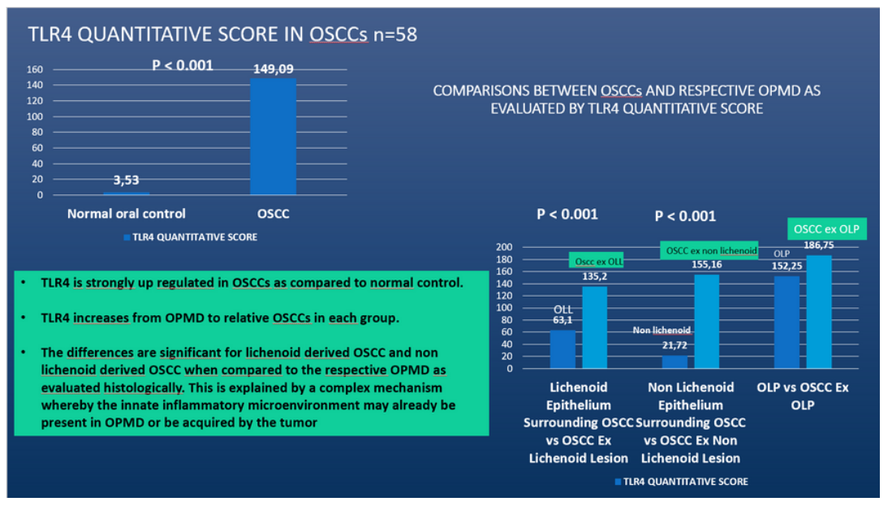
TLR4 EVALUTATION METHODS

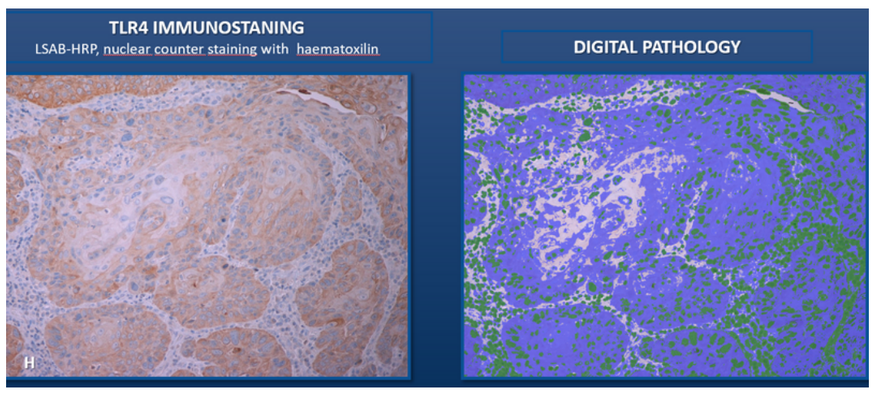
- *TLR4 staining intensity (0-3)*
- *TLR4 percentage of stained cells (0-100)*
- *TLR4 quantitative score (intensity x percentage; 0-300)*
- *TLR4 localization in OPL (1: basal; 2: basal + intermediate; 3: full thickness)*

GRAPHS & TABLES RESUS









RESULTS

TLR-4 wasupregulated in OLP and in OLL and in OSCC ascompared to control groups. Highestvalueswerefound in OLP group (7.06 ± 2.24); progressively, therewereOSCCs ex OLP group (6.38 ± 1.89). Statisticallysignificantdifferenceswereassessed on quantitative score among pathological groups compared with control groups (p<.001). Correlationbetween TLR4 expressionwasinvestigated by Pearson's, showingsignificantrelationship in OLP and OSCC ex OLP group (p = .001).

CONCLUSION

Wefoundsignificant TLR-4 overexpression in OLP, and associationbetween TLR4 and OLP-relatedOSCCs. Collectively, our data support a criticalrole for the host-microbial interactions and TLR4 in OLP pathogenesis, and lichen-relatedoralcarcinogenesis. Drugsdirectedagainstspecific targets suchas PD1 / PD-L1 hasintroduced a significant clinical improvement, and the modulationinflammatory pathway by TLR may be a key factor linking inflammation and tumordevelopment. Furtherour study, haveshown the possibility of identifying an immunologicalsubgroup of oral carcinoma related to the innate-immune pathway, which isassociated to CD8+(low), PD-L1 (low), inhibition of apoptosis and autophagy. Thissubgroup, appearsdistinct from the PD-L1 (hight) group whichisinsteadassociated with CD8(high), with pathways of inflammation, invasion, cellproliferation, vascular and lymphaticneoangiogenesis. TLR-4(high) asdemonstrated in OLP/OLL deriving OSCC, couldthereforeidentify a differentimmunologicalsubgroup, able to allow the cell to survive in a hostileenvironmentsuchasduringinfectiveinflammation.

REFERENCES

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