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Annotated protein network analysis linking oral diseases

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Abstract:
Oral cancer is becoming more common, and it threatens to be a serious worldwide medical issue. Hence, it is of interest to elucidate the networks between proteins and biologically active compounds, as well as their functional annotations, and cell signaling pathways. The online STRING software was used to create a molecular genetics interaction network named AZURIN on oral bacterial proteins. We also used the cystoscope software to identify 11 nodes and 16 edges with an average node order of 2.91. Thus, we document data on the interaction of protein networks with other proteins for identifying potential therapeutic drug candidates linked to oral disease.

Keywords: Networking, STRING, oral cancer, bacteria, cystoscope

Background:
Head and neck tumors are one of the 10 most common types of cancer in the world. Oral squamous cell carcinoma (OSCC) in men is the most common cancer of all head and neck squamous cell carcinomas (HNSCC). It accounts for about 90% of oral malignancies and accounts for more than 300,000 newly diagnosed cases each year **[1-3]**. The molecular basis for aggressive OSCC growth and metastasis is still unknown. OSCCs often remain undetected at the high stages associated with high mortality and are therefore associated with high personal and social costs. The 5-year overall survival rate is estimated to be about 50% **[3]**. Therefore, reducing oral cancer mortality requires new targets for early detection and treatment of OSCC. In recent years, the identification of genes associated with complex diseases has become an important issue. Experimental approaches, such as B. genetic linkage association studies **[4],** expression profiling **[5],** and genome-wide association studies **[6],** are for genes at high relative risk for diseases such as cancer **[7]** and asthma **[8]**. It is successful in identifyingDiabetes **[9]** and hypertension **[10]**. However, disease heterogeneity, the complexity of finding genes at specific loci, and the associated costs have led to the development of various *in-silico* approaches to the identification of diseased genes. The correlation between a particular bacterium and various diseases, including cancer, is well known and well known. The role of bacteria in some types of cancer has been elucidated in more recent studies but remains unclear in many other studies **[11]**. Assessing the dynamics of a microbial population under a medical condition helps determine the mechanisms by which bacteria can be used to induce or develop cancer. Periodontal disease is caused by a bacterial infection of the periodontal tissue that causes gingival inflammation and periodontal disease. Periodontitis affects the gingival tissue but not the underlying tooth support structure. Periodontal disease, in contrast, it's an inflammatory disease that extends deep into the tissue and results in the loss of supporting connective tissue. Periodontitis can lead to loss of connective tissue and bone support and is the leading cause of tooth loss in adults **[12]**. Caries are the destruction of tooth structure by oral bacterial acids produced by microbial fermentation of leftover food **[13]**. Three characteristics of bacterial species are involved in biofilm formation, acid production, and caries development, including acid resistance **[14]**. Many acid-forming and acid-forming bacteria are involved in the carrier, including Streptococcus mutans and Streptococcus sorbinus (collectively known as mutans Streptococcus), as well as other acidic strains of lactobacillus and non-mutans streptococcus **[15]**. This study follows an observational study design aimed at screening for virulence factors in the oral microflora with these proteins ororal cancer and chewing tobacco complex pathogens. This can probably interact with certain proteins. The interaction of oral cancer protein cross-linking with oral mediator proteins and other proteins was analyzed using the STRING v.5 pipeline (Szklarcz) **[16]**. Therefore, it is of interest to document the annotated protein network analysis linking oral diseases.

Methodology:
Sources and selection of the targeting protein
The source of the plant, the geographic location of the collection, the chemical structure, and the biological activity of the oral bacterial protein azurin and oral cancer cyclin B1 protein were obtained from

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bibliographic sources, The origin of the plant, the geographic location of the collection, the chemical structure and biological activity of the oral bacterial proteins azurin and oral cancer cyclin B1 proteins were obtained from bibliographic sources including major journals, masters and papers, chapters of natural product chemistry. The standards used are described by Kumar *et al.* **[17]** and Gupta *et al.* **[18]**.

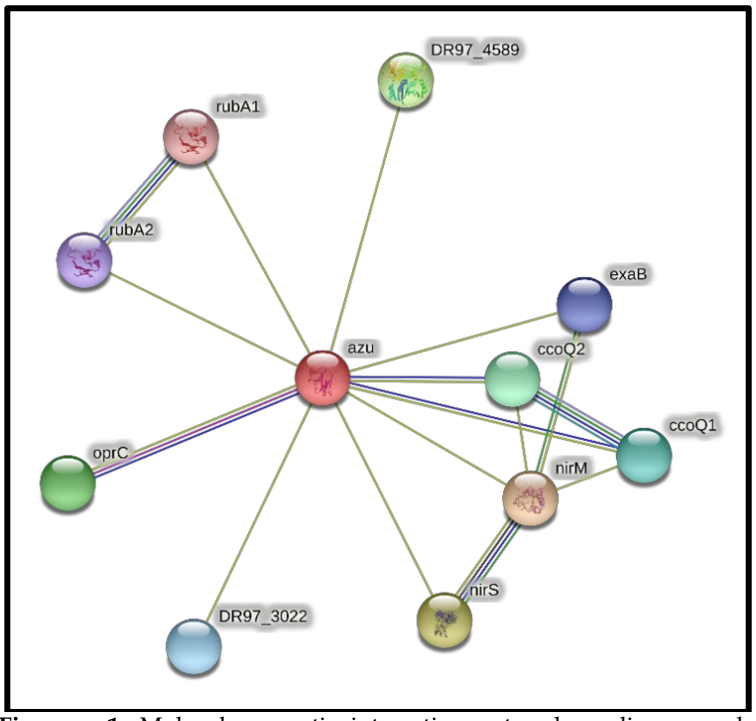

Figure s 1: Molecular genetic interaction network azulin on oral bacterial proteins

Protein and compounds network interaction:

Extensive network analysis is used to identify functional connections between proteins and emphasize the biological importance of genes linked to enrichment pathways. The STRING and STITCH (version: 11.0) databases are global resources for predicting functional connections between proteins and cloud cluster networks and are used to study the interactions between proteins encoded by specific genes. Experiments to identify species using P proteins and chemicals as input gene sets are completed **[19]**. Study protein interactions (PPIs) between enriched genes and networks of interactions between them. A full score above 0.7 indicates a high level of confidence in the presence of significant interactions.

Results and Discussion:

Protein-protein interactions are a central part of the cell network and are known to have many effects. Analyze the information flow network between all target proteins to determine the amount of information that flows between cytochrome proteins and other proteins. Use online STRING software to create a molecular genetic interaction network azulin on oral bacterial proteins, and use Cytoscape software to get 11 nodes, 16 edges, an average node order of 2.91, and visualization averages. I calculated. The local clustering factor is 0.876, the expected number of edges is 10, and the enrichment ppi has a p-value of 0.0553. Nodes, lines, and colors show the rationality of interactive networks (**Figure** 1) (**Table** 1).

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Table 1: Enrichment pathways and linked genes and nodes

Parameter	Value
Number of nodes	11
Number of edges	16
Average node degree	2.91
Avg. local clustering coefficient	0.876
Expected number of edges	10
PPI enrichment p-value	0.0553

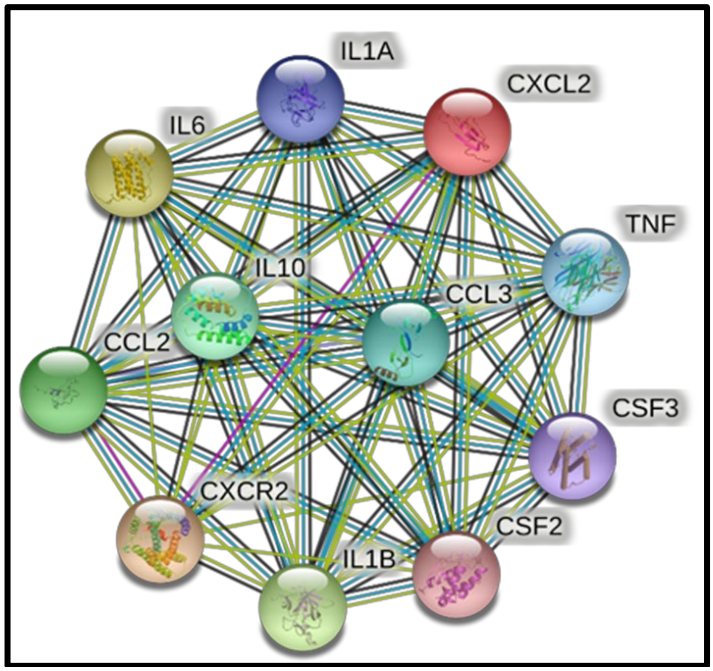

Figure s 2: Oral cancer proteins, interactive network proteins such as CCL2, CCL3, CSF2, IL10, IL1A, IL1B, IL6, TNF, IL10.

For interleukin 8 in oral squamous cell carcinoma, a molecular genetic interaction network was obtained and the software Cytoscape was used to visualize the number of nodes 11, the number of edges 55, the average node order 10, and the values. It was made into. The local clustering factor is 1, the expected number of edges is 20, and the enrichment p-value is ppi 3.25e11 (**Figure** 2) (**Table** 3). Nodes, lines, and colors prove the rationality of interactive networks. Many experiments have shown that the gene is associated with protein expression. The results show that more residues than the cytochrome-protein cross-linking pathway are involved in protein signal intensity.

The result is represented by the color displayed in the forecast tree. A random machine learning approach **[20]** was used to build a reliable

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Bioinformation 18(8): 724-729 (2022)

PPI network by combining co-movement scores obtained from metabolic partitions with detailed information suggesting physical links (**Figure** 2A).This is because physically interacting proteins exert similar biological activity, co-express, and often have similar evolutionary conservation. Only protein pairs with solid biochemical evidence (at least 0.4 correlation rating) from the fractionated dataset were used, and other supporting features were implemented in this subset. Two additional measurements were recorded from biochemical fractional records that reflect reproducibility. Specifically, there are several fractionation experiments in which the co-migration assessment of the protein pair is at least 0.4, and several fractionation experiments with the largest peak in each migration profile. Duplicate protein pairs. Other evidence supporting functional associations is co-[deletion]**[21-23]** interacting domains **[24,25]**, co-evolution **[26]** and phenotypic records **[26]** (**Table** 3). Machine learning classifiers trained on a gold standard set containing only experimentally determined bacterialazulin proteins rubA2, rubA1, oprC, nirS, nirS, nirM, exaB, exaB, ccoQ2, ccoQ1, rubA1, azu, nirM, exaBand tested. (**Table** 2) is responsible for the annotated interactions in the STRING database **[18]**. Interactive network proteins such as CCL2, CCL3, CSF2, IL10, IL1A, IL1B, IL6, TNF and IL10 are shown among oral cancer proteins. Assessment of the relative contribution of each property to PPI prediction (measured by GiniScore) confirmed that the combined biochemical evidence had the greatest effect on classification (**Table** 4) and was associated with other functional associations. Compared to better co-mobility, it shows that it reflects information and is used to predict interactions.

Table 3: Enrichment pathways and linked genes and nodes

Parameter	Value
Number of nodes	11
Number of edges	55
Average node degree	10
Avg. local clustering coefficient	1
Expected number of edges	20
PPI enrichment p-value	3.25E-11

Table 2: Networking of Azurin in oral bacterial protein with annotation

Node1	Node2	Node1 annotation	Node2 annotation	Score
RubA2	RubA1	Involved in the hydrocarbon hydroxylating system	which transfers electrons from NADH to rubredoxin reductase and then through rubredoxin to alkane 1 monooxygenase	0.498
RubA2	Azu	Azu transfers electrons from NADH to rubredoxin reductase and then through rubredoxin to alkane 1 monooxygenase	Transfers electrons from cytochrome c551 to cytochrome oxidase	0.685
RubA1	RubA2	Involved in the hydrocarbon hydroxylating system	It transfers electrons from NADH to rubredoxin reductase and then through rubredoxin to alkane 1 monooxygenase	0.498
RubA1	Azu	It transfers electrons from NADH to rubredoxin reductase and then through rubredoxin to alkane 1 monooxygenase	Transfers electrons from cytochrome c551 to cytochrome oxidase	0.680
OprC	Azu	Putative copper transport outer membrane porin OprC; tonB-copper: TonB-dependent copper receptor	Transfers electrons from cytochrome c551 to cytochrome oxidase	0.762
NirS	NirM	Annotation not available	Electron donor for cytochrome cd1 in nitrite and nitrate respiration	0.984
NirS	Azu	Annotation not available	Transfers electrons from cytochrome c551 to cytochrome oxidase	0.855
NirM	NirS	Electron donor for cytochrome cd1 in nitrite and nitrate respiration	annotation not available	0.984
NirM	ExaB	Electron donor for cytochrome cd1 in nitrite and nitrate respiration	Is an essential component of the ethanol oxidation system that allows P.aeruginosa to grow on ethanol as the sole carbon and energy source.	0.691
NirM	CcoQ2	Electron donor for cytochrome cd1 in nitrite and nitrate respiration	Annotation not available	0.874
NirM	CcoQ1	Electron donor for cytochrome cd1 in nitrite and nitrate respiration	Annotation not available	0.853
NirM	Azu	Electron donor for cytochrome cd1 in nitrite and nitrate respiration	Transfers electrons from cytochrome c551 to cytochrome oxidase	0.968
ExaB	NirM	Is the direct contact between electron acceptor of the quinoprotein ethanol dehydrogenase (QEDH)	Electron donor for cytochrome cd1 in nitrite and nitrate respiration	0.691
ExaB	Azu	the direct electron acceptor of the quinoprotein ethanol dehydrogenase (QEDH)	Transfers electrons from cytochrome c551 to cytochrome oxidase	0.692
CcoQ2	NirM	Annotation not available	Electron donor for cytochrome cd1 in nitrite and nitrate respiration	0.874
CcoQ2	CcoQ1	Annotation not available	annotation not available	0.872
CcoQ2	Azu	Annotation not available	Transfers electrons from cytochrome c551 to cytochrome oxidase	0.741
CcoQ1	NirM	Annotation not available	Electron donor for cytochrome cd1 in nitrite and nitrate respiration	0.853
CcoQ1	CcoQ2	Annotation not available	annotation not available	0.872
CcoQ1	Azu	Annotation not available	Transfers electrons from cytochrome c551 to cytochrome oxidase	0.737

Table 4: Networking of interleukin 8 in oral squamous cell carcinoma with annotation

Node1	Node2	Node1 annotation	Node2 annotation	Score
CCL2	CCL3	May be involved in the recruitment of monocytes into the arterial wall during the disease process of atherosclerosis; Belongs to the intercrine beta (chemokine CC) family	Binds to CCR1, CCR4 and CCR5. One of the major HIV-suppressive factors produced by CD8+ T-cells. Recombinant MIP-1-alpha induces a dose-dependent inhibition of different strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV); Belongs to the intercrine beta (chemokine CC) family	0.921
CCL2	CSF2	Chemotactic factor that attracts monocytes and basophils but not neutrophils or eosinophils. Augments monocyte anti-tumor activity.	Granulocyte-macrophage colony-stimulating factor; Cytokine that stimulates the growth and differentiation of hematopoietic precursor cells from various	0.988

		Belongs to the intercrine beta (chemokine CC) family	lineages, including granulocytes, macrophages, eosinophils and erythrocytes; Belongs to the GM-CSF family	
CCL2	CSF3	C-C motif chemokine 2; Chemotactic factor that attracts monocytes and basophils but not neutrophils or eosinophils. Augments monocyte anti-tumor activity.	Granulocyte colony-stimulating factor; Granulocyte/macrophage colony-stimulating factors are cytokines that act in hematopoiesis by controlling the production, differentiation, and function of 2 related white cell populations of the blood, the granulocytes and the monocytes-macrophages. This CSF induces granulocytes; Belongs to the IL-6 superfamily	0.984
CCL2	CXCL2	Belongs to the intercrine beta (chemokine CC) family	Hematoregulatory chemokine, which, in vitro, suppresses hematopoietic progenitor cell proliferation. GRO-beta(5-73) shows a highly enhanced hematopoietic activity	0.984
CCL2	CXCR2	Has been implicated in the pathogenesis of diseases characterized by monocytic infiltrates, like psoriasis, rheumatoid arthritis or atherosclerosis. Belongs to the intercrine beta (chemokine CC) family	C-X-C motif chemokine 2; Produced by activated monocytes and neutrophils and expressed at sites of inflammation. Binds to IL-8 with high affinity. Also binds with high affinity to CXCL3, GRO/MGSA and NAP-2	0.929
CCL2	IL10	C-C motif chemokine 2; Chemotactic factor that attracts monocytes and basophils but not neutrophils or eosinophils. Augments May be involved in the recruitment of monocytes into the arterial wall during the disease process of atherosclerosis; Belongs to the intercrine beta (chemokine CC) family	Interleukin-10; Inhibits the synthesis of a number of cytokines, including IFN-gamma, IL-2, IL-3, TNF and GM-CSF produced by activated macrophages and by helper T-cells; Belongs to the IL-10 family	0.989
CCL2	IL1A	Augments monocyte anti-tumor activity. Has been implicated in the pathogenesis of diseases characterized by monocytic infiltrates, like psoriasis, rheumatoid arthritis or atherosclerosis.	IL-1 proteins are involved in the inflammatory response, being identified as endogenous pyrogens, and are reported to stimulate the release of prostaglandin and collagenase from synovial cells	0.983
CCL2	IL1B	Has been implicated in the pathogenesis of diseases characterized by monocytic infiltrates, like psoriasis, rheumatoid arthritis or atherosclerosis.	Promotes Th17 differentiation of T-cells	0.993
CCL2	IL6	Chemotactic factor that attracts monocytes and basophils but not neutrophils or eosinophils.	Plays an essential role in the final differentiation of B-cells into Ig- secreting cells Involved in lymphocyte and monocyte differentiation. Acts on B-cells, T-cells, hepatocytes, hematopoietic progenitor cells and cells of the CNS.	0.994
CCL2	TNF	Augments monocyte anti-tumor activity.	it can stimulate cell proliferation and induce cell differentiation. Impairs regulatory T-cells (Treg) function in individuals with rheumatoid arthritis via FOXP3 dephosphorylation. Upregulates the expression of protein phosphatase 1 (PP1), which de [...]	0.992
CCL3	CCL2	Monokine with inflammatory and chemokinetic properties. Binds to CCR1, CCR4 and CCR5. One of the major HIV-suppressive factors produced by CD8+ T-cells. Recombinant MIP-1-alpha induces a dose-dependent inhibition of different strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV); Belongs to the intercrine beta (chemokine CC) family	Tumor necrosis factor; Cytokine that binds to TNFRSF1A/TNFR1 and TNFRSF1B/TNFBR. It is mainly secreted by macrophages and can induce cell death of certain tumor cell lines. It is potent pyrogen causing fever by direct action or by stimulation of interleukin-1 secretion and is implicated in the induction of cachexia, Under certain conditions	0.921
CCL3	CSF2	C-C motif chemokine 3; Monokine with inflammatory and chemokinetic properties. Binds to CCR1, CCR4 and CCR5. One of the major HIV-suppressive factors produced by CD8+ T-cells. Recombinant MIP-1-alpha induces a dose-dependent inhibition of different strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV); Belongs to the intercrine beta (chemokine CC) family	Granulocyte-macrophage colony-stimulating factor; Cytokine that stimulates the growth and differentiation of hematopoietic precursor cells from various lineages, including granulocytes, macrophages, eosinophils and erythrocytes; Belongs to the GM-CSF family	0.988
CCL3	CSF3	Monokine with inflammatory and chemokinetic properties. Binds to CCR1, CCR4 and CCR5. One of the major HIV-suppressive factors produced by CD8+ T-cells. Recombinant MIP-1-alpha induces a dose-dependent inhibition of different strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV); Belongs to the intercrine beta (chemokine CC) family	Granulocyte colony-stimulating factor; Granulocyte/macrophage colony-stimulating factors are cytokines that act in hematopoiesis by controlling the production, differentiation, and function of 2 related white cell populations of the blood, the granulocytes and the monocytes-macrophages. This CSF induces granulocytes; Belongs to the IL-6 superfamily	0.986
CCL3	CXCL2	C-C motif chemokine 3; Monokine with inflammatory and chemokinetic properties. Binds to CCR1, CCR4 and CCR5. One of the major HIV-suppressive factors produced by CD8+ T-cells. Recombinant MIP-1-alpha induces a dose-dependent inhibition of different strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV); Belongs to the intercrine beta (chemokine CC) family	C-X-C motif chemokine 2; Produced by activated monocytes and neutrophils and expressed at sites of inflammation. Hematoregulatory chemokine, which, in vitro, suppresses hematopoietic progenitor cell proliferation. GRO-beta (5-73) shows a highly enhanced hematopoietic activity	0.983
CCL3	CXCR2	Binds to CCR1, CCR4 and CCR5. One of the major HIV-suppressive factors produced by CD8+ T-cells. Recombinant MIP-1-alpha induces a dose-dependent inhibition of different strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV); Belongs to the intercrine beta (chemokine CC) family	C-X-C chemokine receptor type 2; Receptor for interleukin-8 which is a powerful neutrophil chemotactic factor. Binding of IL-8 to the receptor causes activation of neutrophils. This response is mediated via a G-protein that activates a phosphatidylinositol-calcium second messenger system. Binds to IL-8 with high affinity. Also binds with high affinity to CXCL3, GRO/MGSA and NAP-2	0.899
CCL3	IL10	C-C motif chemokine 3; Monokine with inflammatory and chemokinetic properties. Binds to CCR1, CCR4 and CCR5. One of the major HIV-suppressive factors produced by CD8+ T-cells. Recombinant MIP-1-alpha induces a dose-dependent inhibition of different strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV); Belongs to the intercrine beta (chemokine CC) family	Interleukin-10; Inhibits the synthesis of a number of cytokines, including IFN-gamma, IL-2, IL-3, TNF and GM-CSF produced by activated macrophages and by helper T-cells; Belongs to the IL-10 family	0.988

CCL3	IL1A	One of the major HIV-suppressive factors produced by CD8+ T-cells.	Interleukin-1 alpha; Produced by activated macrophages, IL-1 stimulates thymocyte proliferation by inducing IL-2 release, B-cell maturation and proliferation, and fibroblast growth factor activity. IL-1 proteins are involved in the inflammatory response, being identified as endogenous pyrogens, and are reported to stimulate the release of prostaglandin and collagenase from synovial cells	0.984
CCL3	IL1B	Recombinant MIP-1-alpha induces a dose-dependent inhibition of different strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV); Belongs to the intercrine beta (chemokine CC) family	Interleukin-1 beta; Potent proinflammatory cytokine. Initially discovered as the major endogenous pyrogen, induces prostaglandin synthesis, neutrophil influx and activation, T-cell activation and cytokine production, B-cell activation and antibody production, and fibroblast proliferation and collagen production. Promotes Th17 differentiation of T-cells	0.996
CCL3	IL6	C-C motif chemokine 3; Monokine with inflammatory and chemokinetic properties. Binds to CCR1, CCR4 and CCR5. One of the major HIV-suppressive factors produced by CD8+ T-cells. Recombinant MIP-1-alpha induces a dose-dependent inhibition of different strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV); Belongs to the intercrine beta (chemokine CC) family	It is a potent inducer of the acute phase response. Plays an essential role in the final differentiation of B-cells into Ig- secreting cells Involved in lymphocyte and monocyte differentiation. Acts on B-cells, T-cells, hepatocytes, hematopoietic progenitor cells and cells of the CNS. Required for the generation of T(H)17 cells. Also acts as a myokine.	0.989
CCL3	TNF	C-C motif chemokine 3; Monokine with inflammatory and chemokinetic properties. Binds to CCR1, CCR4 and CCR5. One of the major HIV-suppressive factors produced by CD8+ T-cells. Recombinant MIP-1-alpha induces a dose-dependent inhibition of different strains of HIV-1, HIV-2, and simian immunodeficiency virus (SIV); Belongs to the intercrine beta (chemokine CC) family	Tumor necrosis factor; Cytokine that binds to TNFRSF1A/TNFR1 and TNFRSF1B/TNFBR. Impairs regulatory T-cells (Treg) function in individuals with rheumatoid arthritis via FOXP3 dephosphorylation. Upregulates the expression of protein phosphatase 1 (PP1),	0.993

Conclusion:

We document preliminary data from a comprehensive analysis of the interaction of protein networks with other proteins that can be used as potential therapeutic drug candidates for the prevention of oral disease.

Conflict of Interests:

There is no conflict of interests among the authors regarding the present publication.

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