Creating an Online Database for Periodontal Disease Biomarkers

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Introduction and Aims

Periodontal disease is characterised by chronic inflammation and destruction of tooth supporting structures. According to the Adult Dental Health Survey in 2009, the prevalence of advanced periodontal disease in the UK population was estimated at 9%, this figure increased to 15% for those over 55 years old. Clearly this is a significant proportion of the population that often require skilled treatment that can be laborious and expensive with a successful outcome largely depending on empowering the patient to maintain their own excellent standard of oral hygiene.

Detecting the presence of periodontal disease clinically is achieved through clinical assessments such as the Basic Periodontal Examination (BPE). The extent of the disease can then be further investigated through full mouth probing charts, measuring clinical attachment loss and using radiography. However, there can be a great deal of variation in this subjective assessment procedure as well as differences in radiographic interpretations. This has led to difficulties in detecting the disease early enough for prevention as well as accurately monitoring its progression. Furthermore, the current diagnostic procedures are insufficient to provide a substantial indicator for patient susceptibility and assessing the activity level of the disease. Consequently, there has been an increased research interest in salivary biomarkers for periodontal disease, with the aim of aiding management clinically as well as innovating novel methods for chair-side detection[1].

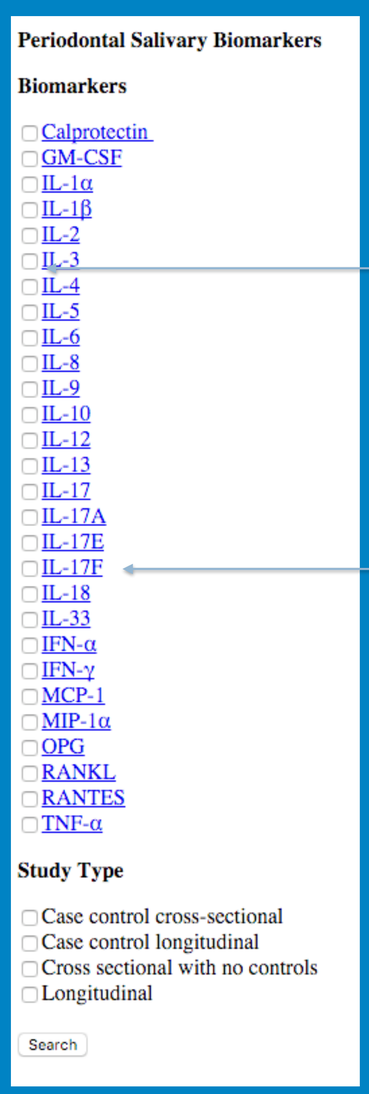
One of the challenges in the field currently is the ability to assimilate and sort through the multifarious and complex literature on the potential biomarkers for periodontitis. The aim of this project is to help address this issue by developing a searchable online database which catalogues studies of salivary biomarkers. We envisage that such a database will enhance the identification and characterisation of candidate biomarkers by researchers in the field. The raw data within the database will originate from a structured review of the literature which was previously undertaken to identify relevant research publications using a Medline search up to September 2014[2]. We will limit the database to studies of saliva in the first instance as this oral fluid is considered the most convenient for clinical sampling.

Methods

The open source relational database management system, MySQL, was used to create the database and a personal secure server used to act as an external host. During the developmental stages, the Apache web page server was used locally which stored all of the folders that contained the PHP files, html files and images. Adobe Dreamweaver was used for all the design work for the front end of the database.

The application was designed to allow for interrogation of the database to collect references based on individual candidate biomarkers investigated (e.g. IL-1ß, TNF-α) and study type (e.g. cross-sectional, longitudinal).

Results 1: Selecting Biomarkers



Tick boxes were used on the front selection page so multiple biomarkers of interest can be selected well as multiple different study types.

Hyperlinks for each individual biomarker link to the GeneCards®: The Human Gene Database. This was included in the instance of a user wanting more comprehensive genetic information regarding biomarkers.

The GeneCards® database can provide the user with comprehensive information on the biomarker, including: aliases, disorders, function, genomics, pathways and variants.

Figure 1. Showing front page option list for functionality testing.

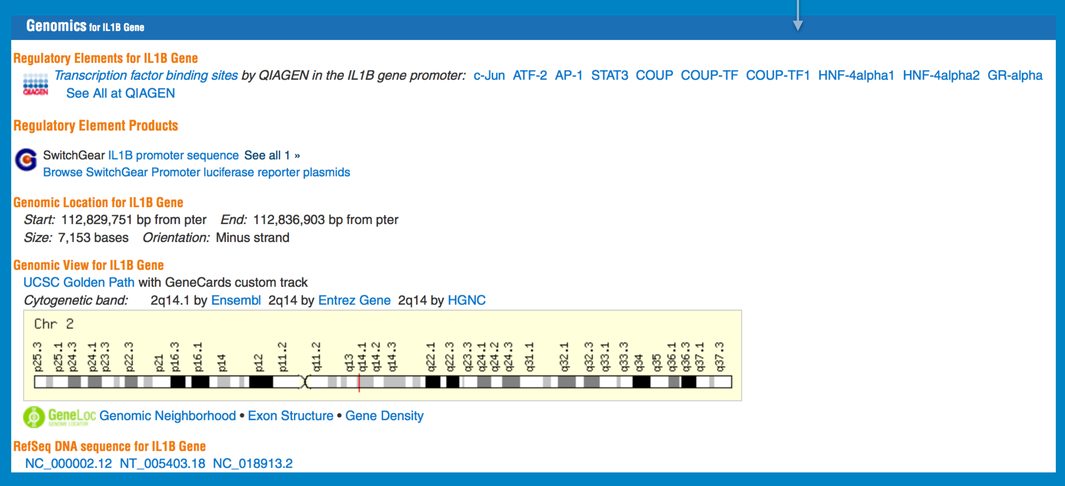


Figure 2. Gene card screenshot example.

Results 2: Search Results Page

A hyperlink leading to the PubMed link to the original paper for reference

The studies are arranged in chronological order

Back to search

PMID	Study	Study Type	Patient Groups	Cytokines Analysed	Principal Findings
16417140	Aurer A, Jorgic-Srdjak K, Plancak D, Stavljenic-Rukavina A, and Aurer-Kozelj J. Coll Antropol 2005: 29: 435-439.	Case control cross-sectional	10 periodontitis patients; 14 healthy controls	TNF-α	TNF-α not detected.
16570465	Miller CS, King CP, Jr., Langub MC, Kryscio RJ, and Thomas MV. J Am Dent Assoc 2006: 137: 322-329.	Case control cross-sectional	28 periodontitis patients; 29 healthy controls	IL-1β, OPG	IL-1β: Significantly higher levels in periodontitis group (mean ± SD; 753.7 ± 1022.4 pg/ml) as compared to controls (212.8 ± 167.4 pg/ml); significant positive correlation with bleeding on probing and clinical attachment loss measurements. OPG: No significant difference between groups.
17435146	Christodoulides N, Floriano PN, Miller CS, Ebersole JL, Mohanty S, Dharshan P, Griffin M, Lennart A, Ballard KL, King CP, Jr., Langub MC, Kryscio RJ, Thomas MV, and McDevitt JT. Ann N Y Acad Sci 2007: 1098: 411-428.	Case control cross-sectional	10 periodontitis patients; 9 healthy controls	IL-1β	No significant difference between groups.
17328758	Ng PY, Donley M, Hausmann E, Hutson AD, Rossomando EF, and Scannapieco FA. FEMS Immunol Med Microbiol 2007: 49: 252-260.	Cross sectional with no controls	98 periodontitis patients	IL-1β, IL-6	IL-1β: Positive association between levels of IL-1β and alveolar bone loss. IL-6: No association with alveolar bone loss.
17435158	Scannapieco FA, Ng P, Hovey K, Hausmann E, Hutson A, and Wactawski-Wende J. Ann N Y Acad Sci 2007: 1098: 496-497.	Case control longitudinal	40 periodontitis patients with bone loss after 5 years; 40 controls with no bone loss	IL-1β, IL-4, IL-6, IL-8, IFN-γ, TNF-α	IL-1β: Positive association with IL-1β and extent of alveolar bone loss over a 5-year period. IL-4, IL-6, IL-8, IFN-γ, TNF-α: No association with alveolar bone loss.
17435158	Scannapieco FA, Ng P, Hovey K, Hausmann E, Hutson A, and Wactawski-Wende J. Ann N Y Acad Sci 2007: 1098: 496-497.	Case control longitudinal	40 periodontitis patients with bone loss after 5 years; 40 controls with no bone loss	IL-1β, IL-4, IL-6, IL-8, IFN-γ, TNF-α	IL-1β: Positive association with IL-1β and extent of alveolar bone loss over a 5-year period. IL-4, IL-6, IL-8, IFN-γ, TNF-α: No association with alveolar bone loss.
18155182	Tobon-Arroyave SI, Jaramillo-Gonzalez PE, and Isaza-Guzman DM. Arch Oral Biol 2008: 53: 346-352.	Case control cross-sectional	28 periodontitis patients; 29 healthy controls	IL-1β	Significantly higher levels in periodontitis group as compared to controls.
18834246	Frodge BD, Ebersole JL, Kryscio RJ, Thomas MV, and Miller CS. J Periodontol 2008: 79: 1913-1919.	Case control cross-sectional	35 periodontitis patients; 39 healthy controls	RANKL, TNF-α	RANKL: Only detected in a minority of subjects and no significant difference between groups. TNF-α: Significantly higher levels in periodontitis group (mean ± SEM; 4.33 ± 0.73 pg/ml) as compared to controls (2.03 ± 0.49 pg/ml).
19210336	Teles RP, Likhari V, Socransky SS, and Haffajee AD. J Periodont Res 2009: 44: 411-417.	Case control cross-sectional	74 periodontitis patients; 44 healthy controls	IL-1β, GM-CSF, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IFN-γ, TNF-α	IL-1β: No significant difference between groups GM-CSF, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IFN-γ, TNF-α: No significant differences between groups for any cytokine. Significant negative correlation between IL-10 levels and bleeding on probing measurements. Significantly positive correlation between IL-8 and bleeding on probing measurements.

Figure 3. Showing an example results page with filters applied for : Il-1B + TNF-a + All study types.

Summary and Future Work

The key for this initial stage of the database was to get the functionality correct and this was successfully achieved. The database has now a platform to grow on from to become a useful resource. The next steps are:

1. Adding design on the front end to make the interface more user friendly
2. Sending out the database to clinical and laboratory scientists as well as postgraduates working in periodontal research within the Centre for Oral Health Research who will trial the database and provide feedback to allow for further development
3. Extend the database to include other mediators e.g. proteases; serum and gingival crevicular fluid in the future. Similarly, we plan to focus on untreated chronic periodontitis as these are fundamental to identifying candidate biomarkers. We could extend our database to include studies of other periodontal diseases e.g. gingivitis and aggressive periodontitis.

Conclusion: A functional database has been created which has the potential to become an excellent resource in periodontal research. This working model now needs to be developed further by sending it out for review by researchers and implementing changes based on their feedback.

References: [1]Katrin M. Jaedicke, Philip M. Preshaw and John J. Taylor Salivary cytokines as biomarkers of periodontal diseases
[2]John J. Taylor and Philip M. Preshaw Gingival crevicular fluid and saliva