CRH_Server: an online comparative and radiation hybrid mapping server for the canine genome

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ABSTRACT

Summary: CRH_Server is an on line Comparative and Radiation Hybrid mapping Server dedicated to canine genomics. CRH_Server allows users to compute their own RH data using the current canine RH map, and allows comparative dog/human mapping analyses. Finally, it suggests multiple options for storage and queries of the dog RH database.


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Supplementary information: All information is available at http://idefix.univ-rennes1.fr:8080/Dogs/help_rh-server.html

Radiation hybrid (RH) maps for the canine species provide a powerful genomic resource for characterizing the canine genome. Radiation hybrid mapping relies on a two-step investigation method that allows the positioning of any marker of interest relative to all other markers along the linear chromosome. The first step involves (PCR) amplification of DNA isolated from a collection of hybrid cell lines. Each cell line carries a portion of the donor species genome, with the entire panel encompassing the genome of the donor several times over (Vignaux \textit{et al}., 1999). The patterns of amplification associated with each marker across the RH panel is termed a ‘vector’. In the second step, RH vectors are submitted to sophisticated statistical treatments that determine the composition of linkage groups, establishing an eventual physical ordering of markers within each linkage group (Ben-Dor \textit{et al}., 1997).

For the dog, the development of genomic tools is well advanced. The current canine 1 Mb resolution RH map comprises 3270 markers (Guyon \textit{et al}., 2003) and additional genomics resources such as a canine BAC library (Li \textit{et al}., 1999), the 1.5× genome sequence (Kirkness \textit{et al}., 2003) and minimal screening sets, MSS1 and MSS2 (Richman \textit{et al}., 2001; Guyon \textit{et al}., 2003), are all publicly available. The construction of dense and accurate RH maps, and the development of efficient analysis algorithms (Agarwala \textit{et al}., 2000; Hitte \textit{et al}., 2003), combined with their on-line availability, is an essential need for a wide spread use of RH maps. We have therefore developed an on-line Comparative and Radiation Hybrid Server (CRH_Server) dedicated to the canine genome analysis. The present RH server allows multiple applications for radiation hybrid analysis, data submission, storage and query coupled with the NCBI MapViewer server tool (Mapview http://www.ncbi.nlm.nih.gov/mapview/map_search.cgi?taxid=9615). The CRH_Server is available at http://idefix.univ-rennes1.fr:8080/Dogs/rh-server.html.

USING THE CRH_SERVER

Radiation hybrid mapping: This is available to determine the linkage of any new marker versus the current canine RH map. Options can be used and combined to specify the query. The output displays (Fig. 1):

(1) Hypertext links for marker(s) linked to the tested marker which allow researchers to obtain corresponding PCR conditions, map positions and characteristics as well as references and online mendelian inheritance in man (OMIM) links for gene-based markers.

(2) Canine chromosomal assignment and coordinates (TSP_units) of the tested marker(s) are provided together with a figure of the relevant chromosome.

(3) The logarithm of the odds (LOD) score and the two-point distance expressed in centiRay5000 between the tested marker and linked marker(s).

(4) The retention level of the tested RH vector is systematically returned.

(5) A possibility of an extended RH analysis search is systematically proposed based on an enlarged RH

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Fig. 1. Example of the output demonstrating linked markers. Top panel shows for BRCA2 submitted marker the significant linkages with adjacent markers reported on 'column 2', their canine chromosomal position 'column 3', LOD value 'column 4', distance in centiRay 'column 5' and human coordinates 'column 6'. Bottom panel shows the comparative dog/human data for BRCA2 submitted marker.

dataset, which is updated daily with recent RH data submissions.

Dog/human comparative mapping: CRH_Server allows investigators to search for syntenic relationships between dog and human genomes from RH vector or queries. The output displays (Fig. 1):

1. Hypertext links for marker(s) linked to the tested marker.
2. The canine chromosomal assignment and coordinates expressed in RH map units for the tested marker(s).
3. Hyperlinks to the MapViewer Server canine database and to the figure (pdf file) of the canine chromosome with the corresponding human chromosome segment(s).
4. Human ortholog sequence coordinates (when known) with hyperlink that returns the 2 Mb human orthologous annotated sequence from the MapViewer Server human database.
5. Conserved dog/human synteny for either the complete dog chromosome or the complete human chromosome identified by the analysis automatically available at the bottom of the Web page.

Combined radiation hybrid mapping and dog/human comparative mapping: This will return all relevant information described above (Fig. 1).

CRH_Server for database submission and storage RH vectors can be submitted through a Web form to be stored in the database. Submitted RH vectors are automatically analyzed and integrated as unverified to the RH dataset and are made available for alternate RH analyses on an enlarged RH dataset daily updated.

Comments: RH analyses can be submitted in batch of markers. The results for the most closely linked marker only
will be returned by email. CRH_Server is developed in awk programming and is hosted on a Sun station SUNFIRE6800. RH mapping calculation uses the rh_tsp_map2.0 package as described by Agarwala et al. (2000).

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REFERENCES


