Helicobacter spp.

Host and bacterial species

Helicobacter spp. have been isolated from a wide range of laboratory animals (Fox & Lee 1997, Whary & Fox 2004). Various bacterial species have been found, and it is expected that additional species colonizing laboratory animals will be described in the near future. In laboratory rodents, the following Helicobacter spp. have been identified:

- mouse: H. muridarum (Lee et al. 1992), 'H. rappini' (Schauer et al. 1993), H. hepaticus (Fox et al. 1994), H. bilis (Fox et al. 1995), H. rodentium (Shen et al. 1997), H. typhlonius (Fox et al. 1999), H. ganmani (Robertson et al. 2001)
- rat: H. muridarum (Lee et al. 1992), H. hepaticus (Riley et al. 1996), H. bilis (Riley et al. 1996), H. trogontum (Mendes et al. 1996), H. rodentium (Goto et al. 2000), H. typhlonius (Livingston & Riley 2003)
- hamster: H. cinaedi (Gebhart et al. 1989), H. cholecystus (Franklin et al. 1996), H. aurati (Patterson et al. 2000), H. mesocricetorum (Simmons et al. 2000)
- Mongolian gerbil: H. bilis (Wang & Fox 1998), H. hepaticus (Goto et al. 2000).

This compilation will focus mainly on H. hepaticus because it is the most prominent of the rodent Helicobacter spp. and is responsible for the most lesions.

Strain susceptibility

Mouse strain differences in disease susceptibility and colonization sites have been reported:

- some mouse strains (including A/JCr, C3H/HeNCr, SJL/NCr, BALB/cAnNCr, and Prkdcscid/NCr) are highly susceptible to H. hepaticus-associated hepatitits, whereas others (C57BL/6NCr, B6C3F1) are resistant (Ward et al. 1994b)
- in aged male A/JCr mice, H. hepaticus infection is linked to the development of liver tumors (Ward et al. 1994b)
- hepatitis-prone A/JCr mice have lower cecal colonization levels of H. hepaticus than hepatitis-resistant C57BL/6 mice (Whary et al. 2001)
- several immunodeficient strains of mice (e.g., Foxn1nu, Prkdcscid, Il10tm1Cgn, Tcratm1Mom) are prone to develop inflammatory bowel disease in response to infections with H. hepaticus (Ward et al. 1996a, Burich et al. 2001), H. bilis (Shomer et al. 1997, Burich et al. 2001), or H. typhlonius (Fox et al. 1999, Franklin et al. 1999)

Organotropism

- lower intestine (primary site)
- stomach (H. muridarum in mice, H. aurati in hamsters)
- liver (H. hepaticus, H. bilis, and H. ganmani in mice)
- gallbladder (H. cholecystus in hamsters)

Clinical disease

- usually inapparent in immunocompetent rodents
- signs of inflammatory bowel disease in immunodeficient mice and rats include rectal prolapse, mild to severe hemorrhagic or watery diarrhea with resultant perianal dermatitis and weight loss (Ward et al. 1996a, Haines et al. 1998, Shomer et al. 1997, Burich et al. 2001)

Pathology

- chronic active hepatitis with focal necrosis and mixed leukocytic infiltrates in mice infected with H. hepaticus (Ward et al. 1994a, Ward et al. 1994b, Fox et al. 1996a) or H. bilis (Fox et al. 1995, Franklin et al. 1998)
- hepatocellular adenoma and carcinoma in H. hepaticus-infected aged A/JCr male mice (Ward et al. 1994b, Fox et al. 1996a)
- proliferative typhlitis, colitis, and proctitis in immunodeficient mice infected with H. hepaticus (Ward et al. 1996a, Burich et al. 2001), H. bilis (Shomer et al. 1997, Burich et al. 2001), or H. typhlonius (Fox et al. 1999, Franklin et al. 1999) and in immunodeficient rats infected with H. bilis (Haines et al. 1998)
- gastritis in H. muridarum-infected mice (Queiroz et al. 1992)
- cholangiofibrosis and centrilobular pancreatitis in H. cholecystus-infected hamsters (Franklin et al. 1996)

Morbidity and mortality

- the incidence and severity of Helicobacter-induced disease depend on strain, gender, and age of the host (Ward et al. 1994b, Fox et al. 1996a, Ward et al. 1996a, Haines et al. 1998, Ihrig et al. 1999, Burich et al. 2001, Livingston et al. 2004

Zoonotic potential

- unclear; some Helicobacter spp. demonstrate zoonotic potential and may cause human disease (e.g., H. cinaedi and 'H. rappini' have been isolated from patients with enteritis and from patients with bacteremia) (De Groote et al. 2000, Andersen 2001)

Interference with research

Physiology

- chronic H. hepaticus infection may lead to elevations in serum levels of alanine aminotransferase (Fox et al. 1996a, Fox et al. 1996b)

Pathology

- H. hepaticus, H. bilis, and H. typhlonius induce or trigger intestinal inflammation in various mouse models of inflammatory bowel disease (Cahill et al. 1997, Kullberg et al. 1998, Fox et al. 1999, Chin et al. 2000, Burich et al. 2001); in contrast, H. hepaticus delays the development of inflammatory bowel disease in multiple drug resistance-deficient mice (Maggio-Price et al. 2002)
- H. muridarum provokes inflammatory bowel disease in Prkdcscid mice reconstituted with CD4+ CD45RBhigh T cells (Jiang et al. 2002)
- H. hepaticus may alter gene expression profiles in the cecum (Myles et al. 2003)

Immunology

- H. hepaticus hepatitis is associated with expression of heat shock protein 70 in the liver and with production of serum antibodies against this protein (Ward et al. 1996b)
- H. hepaticus hepatitis is associated with a Th1 cell-mediated immune response (Whary et al. 1998)
- H. hepaticus and H. bilis increase MHC class II expression and proinflammatory cytokine mRNA expression (skewed towards a Th1 phenotype) in the colons of immunodeficient mice with inflammatory bowel disease (Burich et al. 2001, Kullberg et al. 2001, Tomczak et al. 2003)
- H. hepaticus induces IkB degradation and NF-kB activation in macrophages (Tomczak et al. 2003)

Interactions with other infectious agents

- H. hepaticus may modulate the pathogenesis of mouse hepatitis virus infection (Compton et al. 2003)

Toxicology

- H. hepaticus produces a toxin with granulating cytotoxic activity in mouse liver cells (Taylor et al. 1995) and a cytolethal distending toxin which causes cell distension, accumulation of filamentous actin, and G2/M cell cycle arrest in HeLa cells (Young et al. 2000)

Oncology

- H. hepaticus may alter hepatocellular amd biliary epithelial apoptosis and proliferation indices (Ward et al. 1994a, Fox et al. 1996a, Nyska et al. 1997, Ihrig et al. 1999)
- H. hepaticus hepatitis is associated with increased oxidative DNA damage and overexpression of specific cytochrome P450 isoforms (Sipowicz et al. 1997), epidermal growth factor, transforming growth factor-a, cyclin D1, cyclin-dependent kinase 4, and c-Myc in the liver (Ramljak et al. 1998)
- chronic H. hepaticus infection may increase the incidence of liver tumors (Ward et al. 1994b, Fox et al. 1996a, Hailey et al. 1998) and promote the development and malignancy of liver tumors initiated by chemical carcinogens (Diwan et al. 1997)
- H. hepaticus-driven inflammatory bowel disease may promote colon cancer (Erdmann et al. 2003)
- H. hepaticus can contaminate transplantable tumors (Goto et al. 2001)

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