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# ACCEPTED MANUSCRIPT

# A new magnetic cell fishing approach based on hybridization chain reaction: HCR-MISH

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#### **Highlights**

- Demonstration of the concept of HCR-MISH, a combination of Hybridization Chain Reaction (HCR) with magnetic in situ hybridization (MISH)
- A new cell isolation approach applicable to unculturable bacteria
- An enlarged panel of possible DNA or RNA targets compared to conventional MISH

#### **Abstract**

This paper aims at presenting a new magnetic labeling approach based *on in-situ* hybridization for the specific capture of bacterial cells. This approach is inspired by HCR-FISH, which was recently proposed as a new sensitive method for the detection of environmental microorganisms using a combination of FISH (Fluorescent *In Situ* Hybridization) and HCR (Hybridization Chain Reaction). Here we propose to adapt the technique to allow grafting of superparamagnetic nanoparticles onto target bacteria and therefore to exploit magnetism instead of fluorescence for their subsequent isolation using a micro-magnet array. The feasibility of the approach was first assessed by isolating *E. coli* cells using a universal bacterial probe, Eub338. Then, specific targeting of *Escherichia coli* DH5a, *Pseudomonas putida*, and *Acinetobacter sp.* ADP1 were demonstrated using heterologous probes. For the purpose of comparison, both HCR-FISH and HCR-MISH experimental results are presented.

**Keywords:** Hybridization Chain Reaction ,In situHybridization, Magnetic trapping, micromagnets, bacterial cell isolation

#### Introduction

Culturable bacteria represent only a tiny fraction of the microbial diversity that exists in nature. Nevertheless, a wide range of microorganisms that cannot be grown in the laboratory need to be studied as they play critical roles in environmental processes such as

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