

## Ligand Controlled Hybridization

Specificity • Accuracy

### Introduction

A DNA binding ligand can be defined as any DNA interacting drug or compound which acts to change or modulate the behavior of the DNA with which it comes into contact. Ligands can include DNA binding drugs, such as distamycin, salts of various types (*i.e.*, ammonium ions), organic solvents such as dimethylsulfoxide (DMSO) as well as various peptides and proteins. Tm Bioscience's Ligand Controlled Hybridization (LCH) technology uses ligands in various experimentally determined combinations to modulate specific hybridization reactions. One useful application of LCH are ligands or ligand mixtures which can minimize the level of cross-hybridization in highly parallel hybridization reactions such as DNA microarrays. Decreases in cross-hybridization would minimize the detection of false-positive signals and improve overall analysis accuracy.

### Mismatch Discrimination of Complex Hybridizations using Ligand Mixtures

Tm Bioscience has defined ligands which can significantly decrease the levels of mismatch hybridization among highly homologous sequences. **Figure 1** illustrates the results of a low density DNA microarray experiment. The improvements in hybridization discrimination using the proprietary ligands is evident. Briefly, in the absence of Ligands (**A**), mismatch hybridization on the solid phase is extensive, whereas mismatches drop precipitously in the presence of a ligand discrimination cocktail (**B**). It is notable that the level of the perfect match signal remains high in the presence of the ligands. A graphical representation of the scanned array is shown in **C**. In the absence of ligands, the hybridization signal remains high and is easily discriminated from nonperfect hybrids. It is interesting to note that in the absence of ligands, a relatively high level of mismatched hybrids are formed even when the % similarity of the sequences is low (58%). Analogous performance enhancement is seen in solution phase hybridization formats.

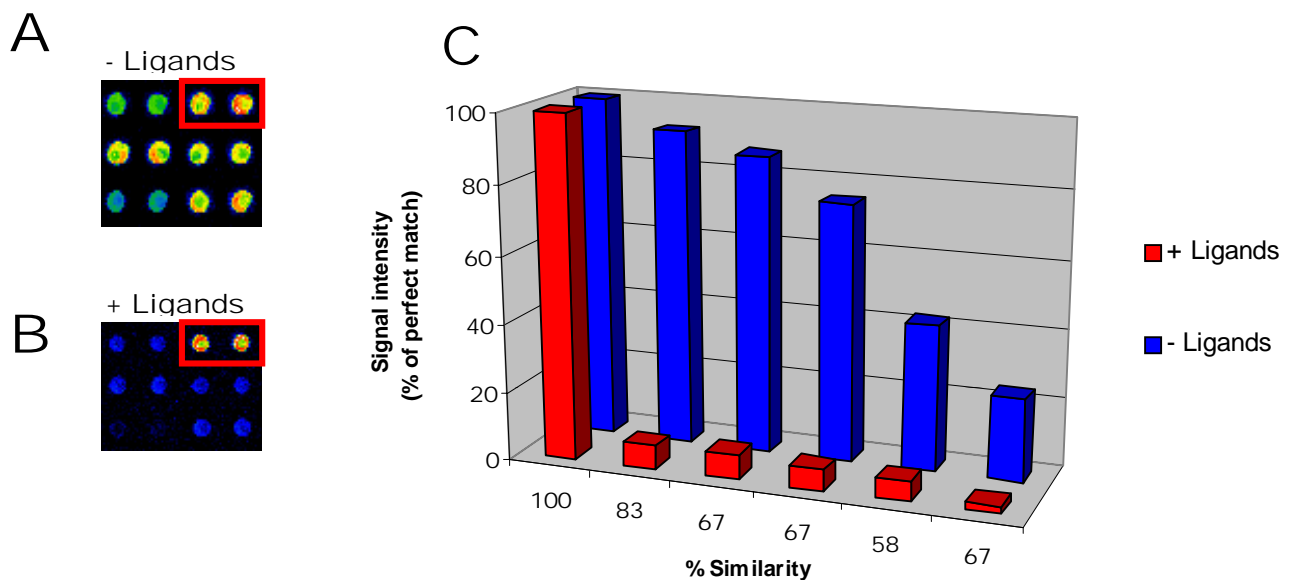


Figure 1: Using Mismatch Discrimination Ligands on DNA microarrays

## **Conclusions**

Tm Bioscience has defined ligands which have the ability to minimize cross-hybridization, or the likelihood of generating false positive signals in both solution and solid phase formats. With this distinctive characteristic, Tm Bioscience's Mismatch Discrimination Ligands provide a powerful solution to problems related to accuracy, consistency and reliability in data obtained from DNA array and non-array platforms.

Other ligand cocktails available from Tm Bioscience Corporation include normalization ligand cocktails.

## **Status**

This technology is covered in part in the following United States patents: No. 5,593,834, 6,027,884 and 6,221,589. Additional patents are pending. Companies interested in licensing this technology or discussing the development of custom ligand cocktails should contact: Dr. Jeremy Bridge Cook, VP Business Development at (416)-593-4323 ext. 229 or by e-mail at [jbridgecook@tmbioscience.com](mailto:jbridgecook@tmbioscience.com).

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