OligoMix® is a versatile, innovative, custom product for genomics discoveries. We synthesize thousands of oligonucleotide sequences in massive parallel on a microarray chip and then cleave the oligos, releasing them into solution in a single microtube. Synthesis occurs via standard DMT chemistry assuring efficient stepwise yield and a high quality final product. The product is delivered as a pool in a single microtube — ready for use in your experiment.

**Economical**
At less than 0.8¢ per base, OligoMix® is about 20 times more cost and time efficient than conventional oligos. Delivered in a single microtube, it enables inexpensive genome-scale experiments.

**Customizable**
Customers can specify each oligonucleotide sequence (lengths up to 150-mers). We can synthesize oligonucleotides in OligoMix® containing labels, such as terminus phosphate, amino and thiol with linkers, biotin, FAM or other dyes.

**Reliable**
Innovative microfluidic array platform ensures high quality synthesis. Multiple QC steps are implemented at various stages of OligoMix® manufacturing. OligoMix is subjected to both hybridization and qRT-PCR assays to assess final quality.

**Simple & Fast**
Download our excel spreadsheet order form, paste in your sequences and email back to us. Product can be delivered in 1-2 weeks.
Sequence Capture Applications

Targeted Sequencing

Though next-generation DNA sequencing (NGS) provides very high levels of coverage, even on complex genomes, it is still advantageous to reduce the complexity of samples and sequence smaller targeted regions – in particular, when sample numbers are very high and the goal is detection of less prevalent mutations. Several academic and commercial groups have developed a variety of capture methods for enriching or selectively amplifying subsets of the genome for targeted sequencing.

The key performance parameters of these methods are capture specificity and sensitivity, the ability to multiplex many samples and capture large regions of interest, and of course, cost. Recently developed methods include: Solution Hybrid Selection (SHS)\(^2,8\), Molecular Inversion Probes (MIP)\(^2,9\), Selective Genomic Circularization (SGC)\(^6,10,11\) and Oligo-Selective Sequencing (OS-Seq)\(^1\). All of these methods have been demonstrated to be effective at selectively enriching desired regions of interest within a given genome.

- **Solution Hybrid Selection (SHS)**\(^2,8\): In vitro transcription of target probes with biotin-UTP. A sequencing library is hybridized to the biotinylated RNA probes in solution and captured targets are recovered with streptavidin beads, and eluted.

- **Molecular Inversion Probes (MIP)**\(^2,9\): Target-specific oligo probe sequences are hybridized to the target region of genomic DNA and the probe is circularized by polymerase and ligase such that the target sequence is incorporated into the circular molecule.

- **Selective Genomic Circularization (SGC)**\(^6,10,11\): The SGC method differs from the MIP-based approach in that the genomic DNA target is directly incorporated into the circular molecules versus the oligo probe being circularized.

- **Oligo-Selective Sequencing (OS-Seq)**\(^1\): In a recently developed targeted capture method, OS-Seq, target-specific oligos modify primers which are immobilized on the sequencing flow cell and function as both a capture and sequencing substrate.

While each method has its own advantages and disadvantages that make them suitable for specific situations\(^5\), the common thread amongst these methods is the need for high quality synthesis of large numbers of oligonucleotide sequences for use as capture probes or primers. This can prove expensive when using conventional solid support column based synthesis methods as the number of sequences can reach into the tens of thousands.

- **It has been demonstrated that the use of microarray synthesized oligos produces the required numbers and quality of oligos quite effectively at a far lower cost**\(^12\).

- **OligoMix\(^\circledR\)** has been demonstrated as an effective method of oligo synthesis for targeted sequencing in MIP\(^2\), SGC\(^6\), and OS-Seq\(^1\) targeted sequencing methods.
Sequence Capture Applications

Targeted Methylation Analysis

As with most genomic analysis methods, CpG methylation analysis must be: quantitative, high-throughput, cost-effective, and both scalable and flexible with respect to coverage. Ideally, one would be able to efficiently investigate the methylation of large numbers of CpGs in large numbers of samples.

The standard method for measuring methylation involves treatment of DNA with sodium bisulfite which causes conversion of unmethylated cytosines (C) to uracils (U), whereas 5-methylcytosine (5mC)s remain unchanged. The differences in reactivity of Cs and SmCs to bisulfite can be distinguished by subsequent microarray\(^5\) or sequencing\(^3,4\) methods.

Both of these methods can benefit from prior targeted capture and amplification of suspected CpG regions in order to reduce the complexity of samples and focus the analysis on specific genomic segments. The use of oligonucleotides for targeted capture increases both sample throughput and coverage, while decreasing cost per sample. Using an OligoMix\(^\circledR\) synthesis strategy vs. individual oligo synthesis further increases flexibility, scalability and cost efficiency of targeted methylation analysis methods. Recently, two new capture methods have been developed for targeted methylation analysis.

One challenge for these methodologies lies in the construction of capture probe panels. They must be customizable to different genomic targets, scalable to a very large sample size (1,000–100,000 samples), and inexpensive. The current procedures are labor intensive and costly, making it impractical for construction of very large panels or custom panels. As a parallel oligo synthesis technology capable of producing virtually unlimited numbers of oligos of lengths up to 100 nucleotides as a pool, OligoMix\(^\circledR\) overcomes this barrier and represents a significantly more cost effective method for construction of probe panels than single-plex PCR.

- Probes generated by OligoMix\(^\circledR\) were compared to single-plex PCR constructed probes using ROC analysis and no significant difference in performance was observed\(^2\).
- Oligo pools therefore represent an inexpensive means for constructing large and custom dU probe panels and greatly improve the flexibility of the assay with respect to coverage.

Library-Free Bisulfite Padlock Probes (BSPPs)\(^3,4\)

In the BSPP sequencing approach, padlock probes are annealed to bisulfite converted genomic DNA, captured targets are circularized then PCR amplified with bar-coded primers and directly sequenced.

Methylation Target Amplification by Capture & Ligation (mTACL)\(^5\)

Digested genomic DNA fragments are mixed with a dU probe panel and common primers, denatured and re-annealed. Captured region are ligated to the primers and reacted with bisulfite, to convert unmethylated cytosines to uracils. The product can be analyzed by microarray or sequencing to detect the presence of U at CpG sites.
<table>
<thead>
<tr>
<th>Product Description</th>
<th>mix of DNA oligonucleotide sequences</th>
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<tbody>
<tr>
<td>Number of Oligos</td>
<td>thousands of sequences or more per tube</td>
</tr>
<tr>
<td>Oligo Form</td>
<td>single stranded (ss); desalted and ready for reaction</td>
</tr>
<tr>
<td>Length</td>
<td>up to 150 mers (inquire for longer oligos)</td>
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<tr>
<td>5’ or 3’ Terminus Modifications</td>
<td>phosphate, fluorescent dyes, biotin, linkers, and others</td>
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<tr>
<td>Internal Modifications</td>
<td>modified DNA or RNA bases</td>
</tr>
<tr>
<td>Yield</td>
<td>*tens of attomoles per sequence and a total of sub-fmols per OligoMix® tube</td>
</tr>
<tr>
<td>Price</td>
<td>(see <a href="http://www.lcsciences.com/discovery/oligomix">www.lcsciences.com/discovery/oligomix</a>)</td>
</tr>
<tr>
<td>Delivery</td>
<td>14 days</td>
</tr>
</tbody>
</table>

**OligoMix® References**


6. LC Sciences’ customers - data unpublished

7. LC Sciences’ internal development work - data unpublished

**Other Oligo Synthesis References**


