

Detecting chemical contaminants via cell bioassays

Cell bioassays have the potential to pick up where traditional contaminant detection and measurement methods leave off

Protecting humans, wildlife and fish from chemical contamination in aquatic environments is a complex management challenge. First, aquatic managers rely on chemistry-based methods to directly monitor specific chemicals; this approach focuses on chemicals that are acutely toxic and trigger severe biological consequences. Second, managers supplement chemical-by-chemical monitoring with toxicology testing, which measures how organisms in a laboratory are affected by cumulative exposure to aquatic contamination.

Although toxicology testing has provided foundational insights into the biological consequences of cumulative contamination exposure, traditional toxicology methods are limited to detecting mortality and impaired growth and reproduction – relatively coarse insights. Traditional toxicology methods also are costly and time-intensive. These limitations have paved the way for the latest advance in toxicology testing: **cell bioassays**.



Cell bioassays enable aquatic samples to be screened for hundreds and perhaps thousands of chemical contaminants that can adversely affect humans, fish and wildlife.

What are cell bioassays?

Cell bioassays are a toxicology testing method for rapidly detecting a wide range of contaminants, including carcinogens, immunosuppressants and endocrine disruptors, that can trigger more subtle, nonlethal health effects. Because cell bioassays monitor for changes at the cellular level, they can detect biological effects that are less pronounced, with results available faster than traditional toxicology and at a lower cost.

Traditional toxicology vs. cell bioassays

Cell bioassays are a valuable complement to traditional toxicology methods, expanding the universe of chemicals that can be monitored.

Traditional toxicology	Cell bioassays
Detects presence of contaminants that cause mortality, impaired growth and impaired reproduction	Detects presence of broad classes of contaminants that cause cellular-level changes linked to cancer, immunosuppression and endocrine disruption
Not sensitive enough to detect low levels of contaminants	Can detect contaminants present at low levels
Uses whole, living organisms	Uses specially engineered, laboratory-grown cells
Typically \$1,000+ per test	Typically hundreds of dollars per test (up to ~\$1,000)
Mid-sized lab can test ~15 samples consecutively	Mid-sized lab can test ~50-100 samples consecutively
Typically takes days to weeks to get results	Typically takes hours (up to two days) to get results

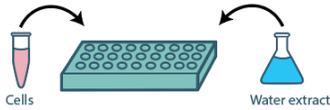
How cell bioassays fit into California's CEC management strategy

California needs a strategy for monitoring the tens of thousands of **contaminants of emerging concern** (CECs) commonly found in aquatic environments that are poorly understood and largely unregulated. Cell bioassays are envisioned as a cost-effective, scalable first line of defense for monitoring a wide range of CECs. Under this new management strategy, which California has begun piloting, aquatic samples are screened for chemical contaminants alongside existing, chemical-specific monitoring methods. Then, depending on findings, more labor-intensive testing methods – including traditional toxicology testing – may be conducted to validate and confirm the findings of cell bioassay testing.

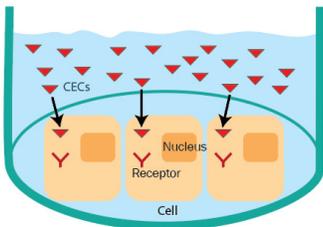
How cell bioassays work

Cell bioassays consist of laboratory-grown cells that react in predictable ways to exposure to chemical contaminants, enabling researchers to gain insights into the biological modes of action by which these contaminants may be adversely affecting the health of fish, wildlife and humans.

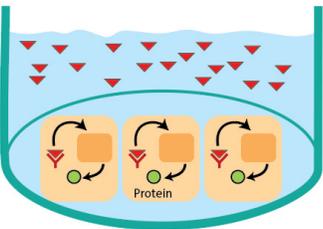
1. Small aliquots of specially engineered cells are combined with a field-collected aquatic sample.



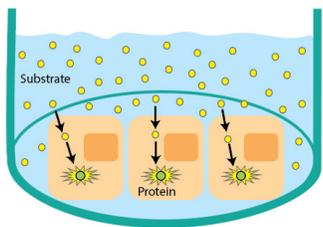
2. Contaminants in the sample are typically given a few hours (or up to 24 hours) to enter the cells and bind to a receptor target inside.



3. Once the contaminants bind to the target receptor, the cells produce a special protein.



4. A substrate is added to the assay that interacts with the protein to produce a light signal.



The strength of the signal reflects the concentration of a specific class of contaminants that the assay is designed to measure.

Do cell bioassays reflect what happens in living animals?

For cell bioassays to be effective as a contaminant screening tool, the changes that happen to a bioassay's cells must reliably reflect the cellular-level changes that would occur in living animals exposed to this same contamination.

Through **linkage studies**, researchers have established that cell bioassays are consistently more sensitive than traditional whole-animal toxicity testing – meaning, cell bioassays are detecting adverse, cellular-level changes before traditional toxicology tests are detecting equivalent changes in living animals. This finding has paved the way for cell bioassays to be used for screening aquatic environments for contaminants, to be followed by more resource-intensive, traditional testing methods.

Developing a battery of cell bioassay tests

Each cell bioassay screens for one major class of chemical contaminants. Researchers are focused initially on adapting cell bioassays to detect three contaminant classes:

Endocrine disruptors

- Estrogen receptor assay*
- Glucocorticoid receptor assay
- Progesterone receptor assay
- Anti-androgen receptor assay

Carcinogens

- Aryl hydrocarbon receptor assay*
- Tumor protein P53 response element assay

Immunosuppressants/neurotoxins

- Thyroid receptor assay
- Peroxisome proliferator activated receptor assay

**Already a monitoring requirement in California for some types of recycled water*

Charting California's path on cell bioassays

California has been experimenting with the use of cell bioassays to screen water bodies in California since the 1980s, although the technology did not gain traction until decades later.

» **Mid-1980s:** Southern California researchers experiment with a cell-based screening test known as the P450 report gene system to understand how polycyclic aromatic hydrocarbons (PAHs) in seafloor sediment in coastal Southern California have adversely affected the health of marine communities; PAHs are a carcinogenic byproduct of burning wood and other fuels.

» **2000s:** The U.S. Environmental Protection Agency and other federal agencies establish that cell bioassays are a viable alternative to animal testing for determining the safety of pesticides and other consumer chemicals. In response, researchers begin examining how to adapt this technology to detect potentially harmful chemical contaminants in aquatic environments.

» **2020:** California develops a policy requiring some types of recycled water to be screened with a pair of bioassays – the estrogen receptor assay and aryl hydrocarbon receptor assay – for an initial four-year period.

» **2021:** The National Water Research Institute releases guidance on how to use cell bioassays to screen recycled water, paving the way for water recycling agencies to begin generating bioassay screening data. The data will help California evaluate whether to pursue development of health risk thresholds that define the inflection point at which levels of bioactive contaminants that have been detected via cell bioassays should trigger prescriptive follow-up actions, such as further investigation or enhanced source-control measures. The European Union already has made progress with threshold development.

More reading

[SCCWRP overview of cell bioassays](#)

[Guidance for using cell bioassays to screen recycled water](#)

