

## NIAID's Framework for Progress on Hepatitis C

RESEARCH GOALS	IMPACT ON PUBLIC HEALTH	STRATEGIES	TACTICAL APPROACHES
UNDERSTAND TRANSMISSION MODES	PREVENT NEW INFECTIONS	<ul style="list-style-type: none"> <li>• identify routes and rates of transmission in multiple settings and populations</li> <li>• develop effective intervention methods</li> </ul>	<ol style="list-style-type: none"> <li>1. identify possible new mechanisms of transmission or that facilitate transmission to include host and viral components</li> <li>2. develop capabilities in special study cohorts and integrate information into overall picture of transmission</li> </ol>
UNDERSTAND PATHOGENIC MECHANISMS AND NATURAL HISTORY	NEW MEANS TO DIAGNOSE AND INTERVENE	<ul style="list-style-type: none"> <li>• identify viral and host factors that contribute to pathogenesis</li> <li>• define mechanisms of viral pathogenesis, i.e., virally induced liver injury</li> <li>• determine timing, identify prognostic factors, and mechanisms of disease progression</li> <li>• identify surrogate markers of disease</li> <li>• determine natural history and outcomes of infection</li> <li>• determine study impact of viral genotypes/ and mutants</li> <li>• determine role of alcohol consumption in progression of HCV disease and characterize underlying mechanism(s)</li> </ul>	<ol style="list-style-type: none"> <li>1. develop capabilities for long-term, multi-disciplinary studies in well-defined, representative human cohorts and include specimen collection for future research opportunities</li> <li>2. facilitate development of infectious cDNA clones and viral pools</li> <li>3. ensure appropriate investigator access to chimpanzee model</li> <li>4. develop <i>in vitro</i> model systems in which to perform some pathogenesis studies</li> <li>5. develop, characterize, and comparatively evaluate model systems of infection and disease, especially small animal model alternatives to the chimpanzee</li> <li>6. exploit appropriate animal models to dissect pathogenesis and study</li> </ol>

			<p>natural history</p> <ol style="list-style-type: none"> <li>7. use research findings to develop new intervention and diagnostic strategies</li> <li>8. derive cost/benefit estimates for different outcomes and the impact of new medical interventions</li> </ol>
<p>CHARACTERIZE HOSTS' IMMUNE RESPONSES TO INFECTION</p>	<p>SAFE AND EFFECTIVE VACCINES TO PREVENT INFECTION AND DISEASE AND IMMUNO-MODULATORY APPROACHES TO DISEASE INTERVENTION</p>	<ul style="list-style-type: none"> <li>• define mechanisms of protective immunity</li> <li>• define neutralizing antibodies to viral antigens</li> <li>• define natural mechanisms and correlates of recovery and persistence</li> <li>• distinguish protective from injury-invoking role of cell-mediated immunity responses</li> <li>• define immunological mechanisms associated with, and identify alterations in response to, repeated infections and co-infections</li> </ul>	<ol style="list-style-type: none"> <li>1. develop capabilities for studies and evaluation in human acute infection cohorts and include specimen collection and repository capabilities</li> <li>2. take advantage of infectious cDNA clones and viral pools</li> <li>3. ensure appropriate investigator access to chimpanzee model</li> <li>4. develop and make available a standardized set of viral reagents for use in evaluation of human immune responses to include HCV antibodies, cDNA clones and confirmation of sequences in databases.</li> <li>5. characterize immune response in the chimpanzee – the only existing model</li> <li>6. develop, characterize, and comparatively evaluate model systems of infection, both tissue culture and small animal models</li> <li>7. exploit appropriate models for immune response research and vaccine evaluation</li> <li>8. provide for detailed, multiple, and</li> </ol>

			<p>iterative vaccine approaches and detailed immune response studies</p> <ol style="list-style-type: none"> <li>9. use basic and clinical research results to devise ever more rational vaccination strategies</li> <li>10. promote development of better methods to study the immune response</li> </ol>
<p>DEFINE VIRAL REPLICATION AND THERAPY STRATEGIES</p>	<p>NEW, SAFE, AND EFFECTIVE THERAPIES TO TREAT INFECTION AND DISEASE</p>	<ul style="list-style-type: none"> <li>• define detailed mechanisms of replication including interactions with the host cell</li> <li>• identify key viral functions</li> <li>• develop understanding of structure and function relationships</li> <li>• define molecular mechanisms and predictors of sustained responses to therapy, i.e., recovery from chronic infection and disease</li> </ul>	<ol style="list-style-type: none"> <li>1. develop in vitro assays for antiviral targets</li> <li>2. enhance development of infectious cDNA clones and viral pools</li> <li>3. ensure appropriate investigator access to chimpanzee model</li> <li>4. develop, characterize, and comparatively evaluate both <i>in vitro</i> and <i>in vivo</i> model systems in which to study replication and antivirals</li> <li>5. use appropriate models (including related Flaviviridae) for replication research, study of recovery parameters and evaluation of therapies</li> <li>6. develop multi-center access to a variety of patient populations and multi-disciplinary capabilities for research based clinical studies and trials and include specimen collection, storage and retrieval prospective development of tools to study viral resistance to antiviral agents</li> <li>7. translate research discoveries into</li> </ol>

			<p>therapy development</p> <p>8. provide for multi-center access to a variety of patient populations and multi-disciplinary capabilities for research based clinical studies and trials and include specimen collection, storage and retrieval to cover future research opportunities and prospective development of tools to study viral resistance to antiviral agents</p>
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