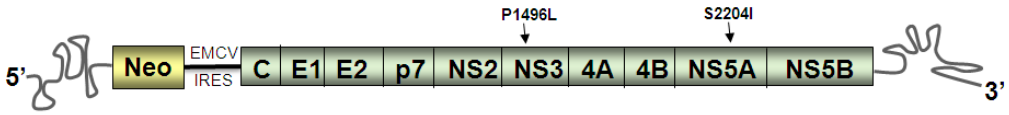
TANGIBLE PROPERTY PORTFOLIO

TERMS:

- Subgenomic replicon—a replicon in which a portion of the viral genome has been deleted; commonly, the structural regions have been deleted, and only NS3 through NS5B are retained within the replicon
- Full-length replicon—a replicon that encodes the entire genome
- Selectable replicon—encodes a marker that allows for the selection of cells that contain the replicon
- Non-selectable replicon—does not encode a marker that allows for the selection of cells that contain the replicon
- HCVcc—hepatitis C virus produced in cell culture
- NTR—non-translated region
- EMCV—Encephalomyocarditis virus
- IRES—internal ribosome entry site
- (see accompanying sheet for schematics)

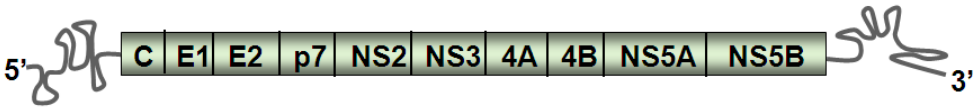
REPLICONS

- Genotype 1
  - Subtype 1a (H77)
    - *Full-length*
      - **Selectable**
        - APP239-- H/FL-Neo (L+I)



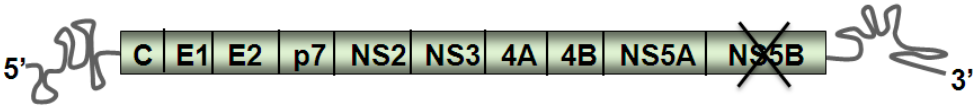
          - Special features: *NS3 (P1496L) and NS5A (S2204I) adaptive mutations*
          - Potential uses: *high throughput screening for replication inhibitors (RNA readout), mechanism of action, replication studies*

      - **Non-selectable**
        - APP243-- H/FL



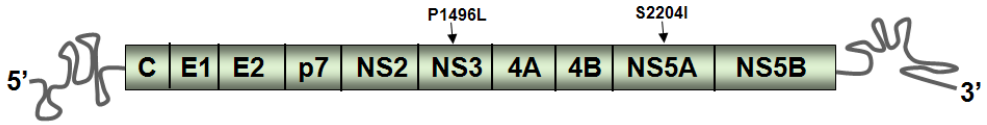
          - Special features: *absence of heterologous elements*
          - Potential uses: *cell culture adaptation*

        - APP290-- H/FL pol-



          - Special features: *replication-deficient polymerase*
          - Potential uses: *replication-incompetent control*

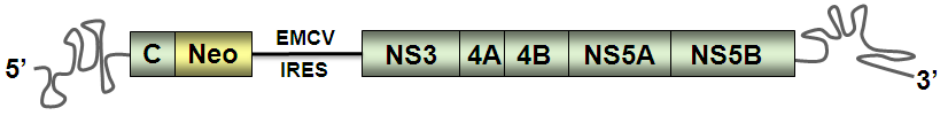
- APP240-- H/FL (L+I)



  - Special features: *absence of heterologous elements, NS3 (P1496L) and NS5A (S2204I) adaptive mutations*
  - Potential uses: *mechanism of action, replication studies*

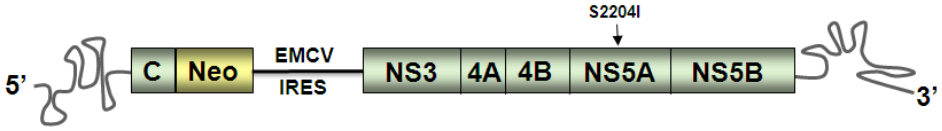
- *Subgenomic*

  - **Selectable**
    - APP241-- H/SG-Neo



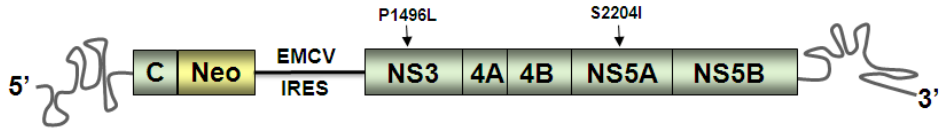
      - Special features: *absence of adaptive mutations*
      - Potential uses: *cell culture adaptation*

    - APP242-- H/SG-Neo (I)



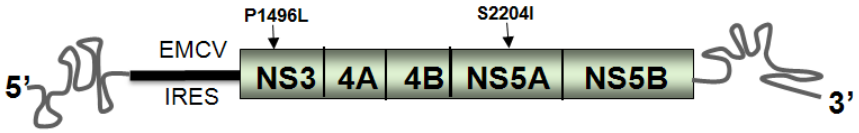
      - Special features: *NS5A (S2204I) adaptive mutation*
      - Potential uses: *cell culture adaptation*

    - APP238-- H/SG-Neo (L+I)



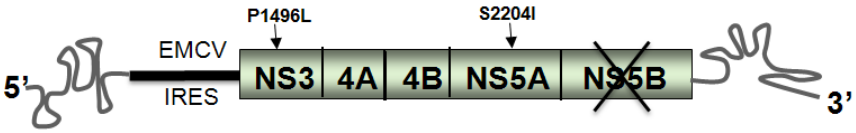
      - Special features: *NS3 (P1496L) and NS5A (S2204I) adaptive mutations*
      - Potential uses: *high throughput screening for replication inhibitors (RNA readout), replicon clearance assay, mechanism of action, replication studies*

  - **Non-selectable**
    - APP245-- H/SG-5'HE (L+I)



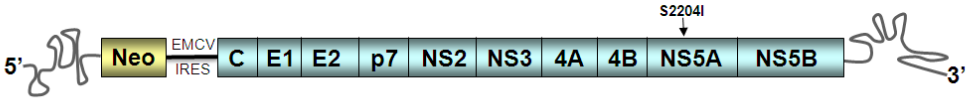
      - Special features: *NS3 (P1496L) and NS5A (S2204I) adaptive mutations; HCV 5' NTR fused to EMCV IRES (designated "HE")*
      - Potential uses: *replication studies*

    - APP251-- H/SG-5'HE (L+I) pol-



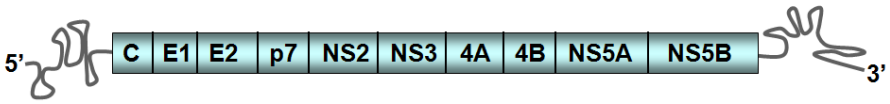
- Special features: *replication-deficient polymerase*
- Potential uses: *replication-incompetent control*

- Subtype 1b (Con1)
  - *Full-length*
    - **Selectable**
      - APP247-- Con/FL-Neo (I)



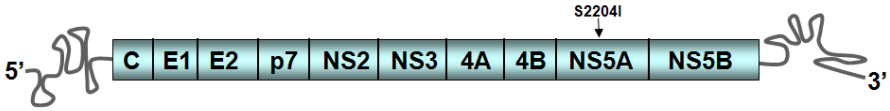
        - Special features: *NS5A (S2204I) adaptive mutation*
        - Potential uses: *high throughput screening for replication inhibitors (RNA readout), mechanism of action, replication studies*

    - **Non-selectable**
      - APP248-- Con1/FL



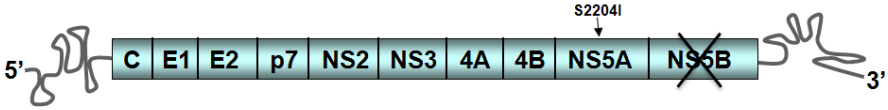
        - Special features: *absence of adaptive mutations*
        - Potential uses: *cell culture adaptation*

      - APP246-- Con1/FL (I)



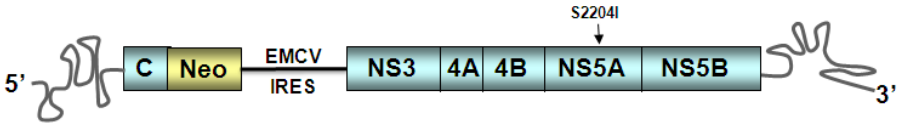
        - Special features: *NS5A (S2204I) adaptive mutation*
        - Potential uses: *mechanism of action, replication studies*

      - APP237-- Con1/FL (I) pol-



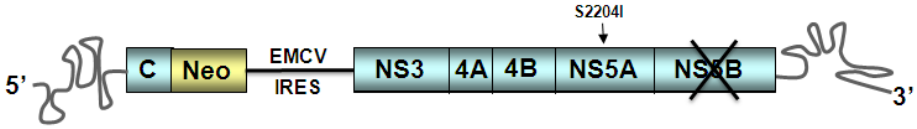
        - Special features: *replication-deficient polymerase*
        - Potential uses: *replication-incompetent control*

  - *Subgenomic*
    - **Selectable**
      - APP203-- Con1/SG-Neo (I)



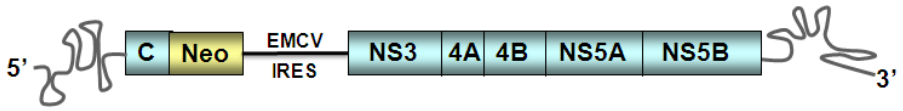
        - Special features: *NS5A (S2204I) adaptive mutation*
        - Potential uses: *high throughput screening for replication inhibitors (RNA readout), replicon clearance assay, mechanism of action, replication studies*

      - APP221-- Con1/SG-Neo (I) pol-



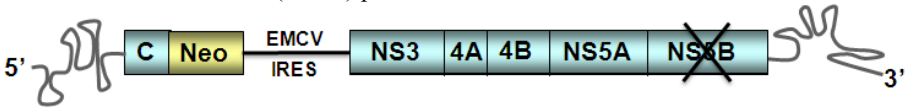
- Special features: *replication-deficient polymerase*
- Potential uses: *replication-incompetent control*

- APP277-- Con1/SG-Neo (AvaII)



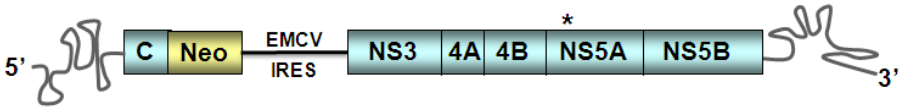
- Special features: *absence of adaptive mutations*
- Potential uses: *cell culture adaptation*

- APP270-- Con1/SG-Neo (AvaII) pol-



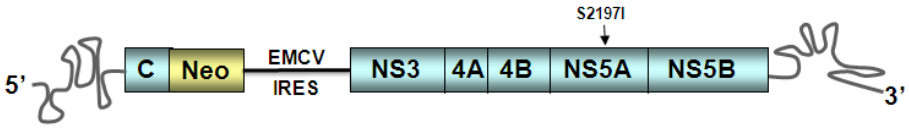
- Special features: *replication-deficient polymerase*
- Potential uses: *replication-incompetent control*

- APP252-- Con1/SG-Neo(delta 47)



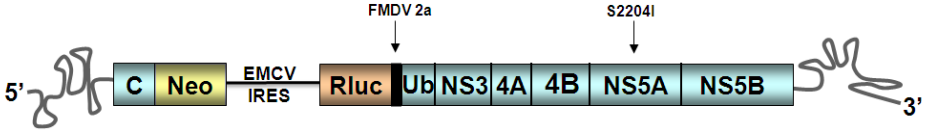
- Special features: *47 amino acid deletion within NS5A*
- Potential uses: *high throughput screening for replication inhibitors (RNA readout), replicon clearance assay, mechanism of action, replication studies*

- APP253-- Con1/SG-Neo(S2197P)



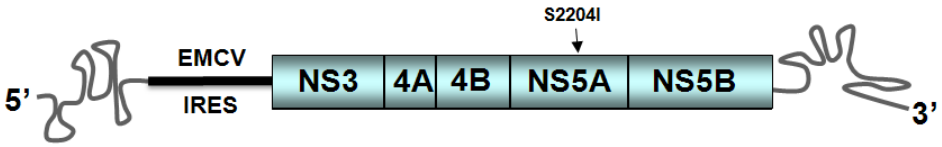
- Special features: *NS5A (S2197P) adaptive mutation*
- Potential uses: *high throughput screening for replication inhibitors (RNA readout), replicon clearance assay, mechanism of action, replication studies*

- APP76-- Con1/SG-Neo(I)hRlucFMDV2aUb



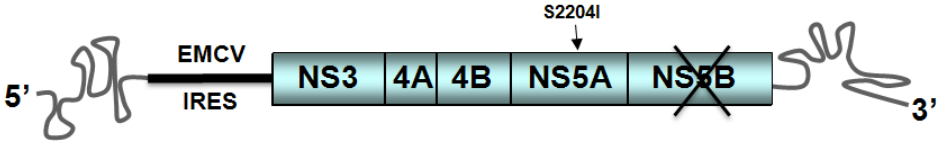
- Special features: *Renilla luciferase reporter, NS5A (S2204I) adaptive mutation*
- Potential uses: *high throughput screening for replication inhibitors (Renilla luciferase readout), replicon clearance assay, mechanism of action, replication studies*

- **Non-selectable**
  - APP249 --Con1/SG-5'HE (I)



- Special features: *NS5A (S2204I) adaptive mutation; HCV 5' NTR fused to EMCV IRES (designated "HE")*
- Potential uses: *replication studies*

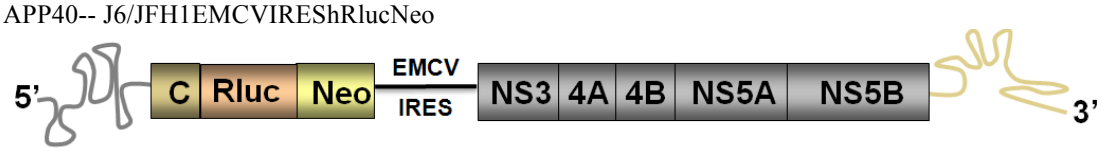
- APP250 --Con1/SG-5'HE (I) pol-



- Special features: *replication-deficient polymerase*
- Potential uses: *replication-incompetent control*

- Genotype 2a (J6, JFH1)
  - Reporter

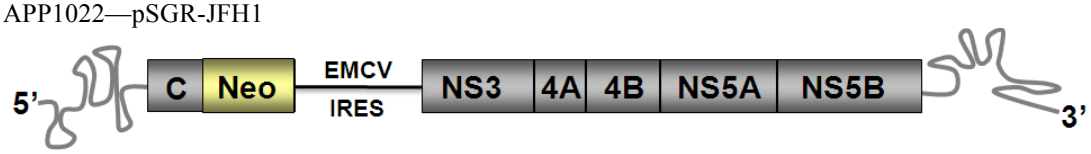
- APP40-- J6/JFH1EMCVIREShRlucNeo



- Special features: *replicon derived from JFH1 except for core and 3' NTR, which are derived from J6 (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
- Potential uses: *high throughput screening for replication inhibitors (Renilla luciferase readout), replicon clearance assay, mechanism of action, replication studies*

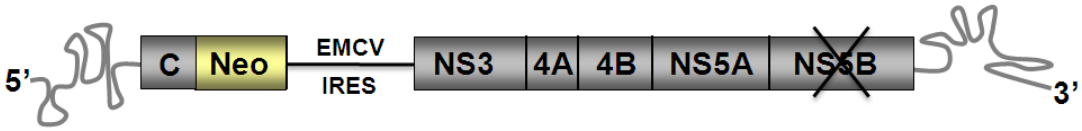
  - Non-reporter

- APP1022—pSGR-JFH1



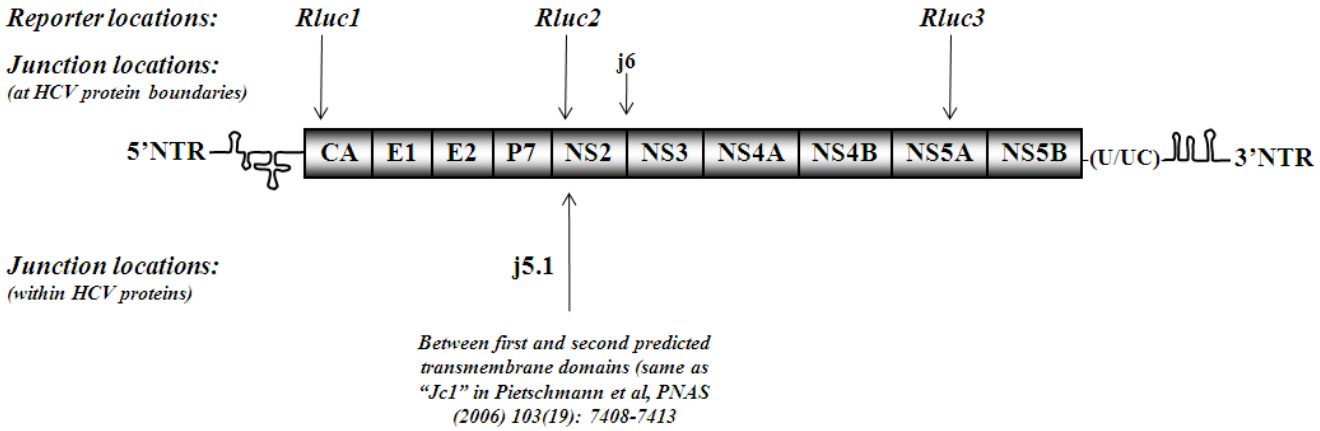
- Special features: *absence of adaptive mutations*
- Potential uses: *high throughput screening for replication inhibitors (RNA readout), replicon clearance assay, mechanism of action, replication studies*

- APP1026—pSGR-JFH1/GND

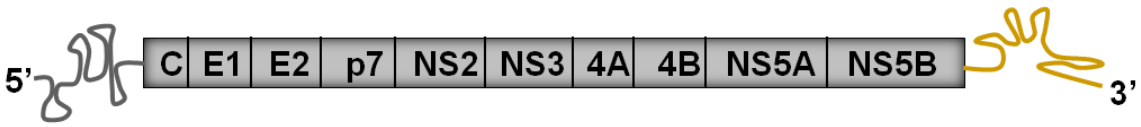


- Special features: *replication-deficient polymerase*
- Potential uses: *replication-incompetent control*

HCVcc

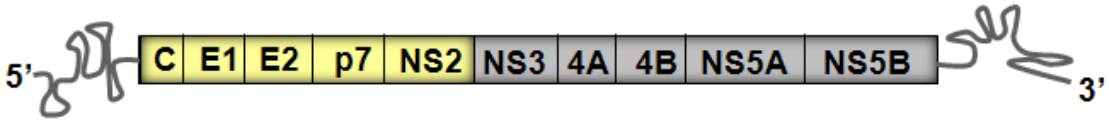


- **Full-length genomes and derivatives**
  - APP36—JFH1



    - Special features: *no adaptive mutations; JFH1 5'NTR, J6 3'NTR* (NOTE: JFH1 and J6 3'NTR differ only in variable region)
    - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 2a (JFH1)*
  - APP1025-- JFH1
    - Special features: *full-length JFH1 genome, no adaptive mutations*
    - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 2a (JFH1)*
  - APP1023—JFH1/GND
    - Special features: *replication-deficient polymerase*
    - Potential uses: *replication-incompetent control*
  - APP1024-- JFH1 delta E1E2
    - Special features: *lacks a portion of E1 and E2 coding regions*
    - Potential uses: *E1- and E2-dependent entry-deficient control*

- **JFH1-based chimeras**
  - **Genotype 1a/2a** ***(shown below with chimeric junction located between NS2 and NS3 (i.e. j6))***



    - ***H77 strain***

      - Non-reporter
        - APP53—H77/JFH (j5.1)
          - Special features: *chimeric junction within NS2; no adaptive mutations; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
          - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1a (H77strain), cell culture adaptation may be desirable*

        - APP99-- H77/JFH (j5.1; Y835H)
          - Special features: *chimeric junction within NS2; Y835H adaptive mutation within NS2 N-terminal to the chimeric junction; JFH1 5'NTR, J6 3'NTR* (NOTE: JFH1 and J6 3'NTR differ only in variable region)
          - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1a (H77strain), further cell culture adaptation may be desirable*

        - APP103-- H77/JFH (j6; I348S, S1107T)
          - Special features: *chimeric junction between NS2 and NS3; E1 (*I348S) *and NS3 (S1107T) adaptive mutations; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
          - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1a (H77strain)*

        - APP104-- H77/JFH (j6; S1107T)
          - Special features: *chimeric junction between NS2 and NS3; NS3 (S1107T) adaptive mutation; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
          - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1a (H77strain)*

        - APP107-- H77/JFH (j6; K12N,I348S,S1107T)
          - Special features*: chimeric junction between NS2 and NS3; core (K12N), E1 (I348S), and NS3 (S1107T) adaptive mutations; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
          - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1a (H77strain)*

        - APP108-- H77/JFH (j6; K12N, S1107T)
          - Special features: *chimeric junction between NS2 and NS3; core (K12N) and NS3 (S1107T) adaptive mutations; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*

- Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1a (H77strain)*

- APP1028-- H77/JFH(j6; V787A, Q1247l)
  - Special features: *chimeric junction between NS2 and NS3; p7 (V787A) and NS3 (Q1247l) adaptive mutations*
  - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1a (H77strain)*

- APP1029-- H77/JFH(j6; R1408W)
  - Special features: *chimeric junction between NS2 and NS3; NS3 (R1408W) adaptive mutations*
  - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1a (H77strain)*

- Reporter

  - *Monocistronic*
    - APP82-- mH77/JFHRluc1 (j5.1; Y835H)
      - Special features: *chimeric junction within NS2; NS2 (Y835H) adaptive mutation within NS2 N-terminal to the chimeric junction; Renilla luciferase reporter fused to N-terminal region of core; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
      - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 1a (H77strain); further cell culture adaptation may be desirable*

    - APP116-- mH77/JFHRluc1 (j6; K12N, S1107T)
      - Special features: *chimeric junction between NS2 and NS3; core (K12N) and NS3 (S1107T) adaptive mutations; Renilla luciferase reporter fused to N-terminal region of core; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
      - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), entry inhibitors of genotype 1a (H77strain); further cell culture adaptation may be desirable*

    - APP1058-- mH77/JFHhRluc3(j6; del, 2 adapt muts)
      - Special features: *chimeric junction between NS2 and NS3; contains two adaptive mutations (confidential information); Renilla luciferase reporter within domain III of NS5A; deletion within NS5A*
      - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout),identification of entry inhibitors of genotype 1a (H77strain)*

  - *Bicistronic*
    - APP115-- biH77/JFHRluc1 (j6; K12N, S1107T)
      - Special features: *chimeric junction between NS2 and NS3; core (K12N) and NS3 (S1107T) adaptive mutations; Renilla luciferase reporter fused to N-terminal region of core; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*

- Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 1a (H77strain); further cell culture adaptation may be desirable*

- Heterologous NS5A
  - APP1118-- H77/JFH(j6; 3 adapt muts; $H77^{NS5A}$)
    - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from H77 strain; contains three adaptive mutations (confidential information))*
    - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- ***TN strain***

  - Non-reporter
    - APP1030-- TN/JFH(j6; V787A, Q1247L)
      - Special features: *chimeric junction between NS2 and NS3; p7 (V787A) and NS3 (Q1247l) adaptive mutations*
      - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1a (TN strain)*

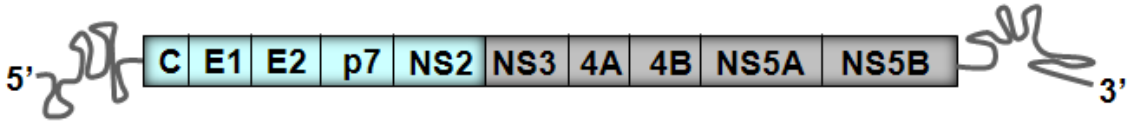
    - APP1031-- TN/JFH(j6; R1408W)
      - Special features: *chimeric junction between NS2 and NS3; NS3 (R1408W) adaptive mutations*
      - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1a (TN strain)*

  - Reporter

    - *Monocistronic*
      - APP1059-- mTN/JFHhRluc3(j6; del, 2 adapt muts)
        - Special features: *chimeric junction between NS2 and NS3; contains two adaptive mutations (confidential information); Renilla luciferase reporter within domain III of NS5A; deletion within NS5A*
        - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 1a (TN strain)*

  - Heterologous NS5A
      - APP1119-- TN/JFH(j6; 2 adapt muts; TN^{NS5A})
        - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from TN strain; contains two adaptive mutations (confidential information))*
        - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- **Genotype 1b/2a** ***(shown below with chimeric junction located between NS2 and NS3 (i.e. j6))***



  - ***Con1 strain***

    - Non-reporter
      - APP55-- Con1/JFH (j5.1)
        - Special features: *chimeric junction within NS2; no adaptive mutations; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
        - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1b (Con1strain), cell culture adaptation may be desirable*

      - APP105-- Con1/JFH (j5.1; Y835C)
        - Special features: *chimeric junction within NS2; Y835C adaptive mutation within NS2 N-terminal to the chimeric junction; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
        - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1b (Con1strain), additional cell culture adaptation may be desirable*

      - APP142-- Con1/JFH (j5.1; 8 adaptive muts)
        - Special features: *chimeric junction within NS2; contains eight adaptive mutations (confidential information); JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
        - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1b (Con1strain)*

      - APP143-- Con1/JFH (j5.1; 7 adapt muts)
        - Special features: *chimeric junction within NS2; contains seven adaptive mutations (confidential information); JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
        - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1b (Con1strain)*

      - APP144-- Con1/JFH (j5.1; 5 adapt muts (-E1E2))
        - Special features: *chimeric junction within NS2; contains five adaptive mutations (confidential information) but lacks adaptive mutations with the envelope proteins; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
        - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1b (Con1strain)*

    - Reporter

      - *Monocistronic*
        - APP110-- mCon1/JFHRluc1 (j5.1)

- Special features: *chimeric junction within NS2; Renilla luciferase reporter fused to N-terminal region of core; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
- Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 1b (Con1 strain); additional cell culture adaptation may be desirable*

▪ APP151-- mCon1/JFHnsGluc2(j5.1; 5 adapt muts (-E1E2))
- Special features: *chimeric junction within NS2; contains five adaptive mutations (confidential information) but lacks adaptive mutations with the envelope proteins; Gaussia luciferase reporter fused C-terminal to the p7/NS2 junction; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
- Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Gaussia luciferase readout), identification of entry inhibitors of genotype 1b (Con1 strain)*

▪ APP152-- mCon1/JFHRluc2(j5.1; 5 adapt muts (-E1E2))
- Special features: *chimeric junction within NS2; contains five adaptive mutations (confidential information) but lacks adaptive mutations with the envelope proteins; Renilla luciferase reporter fused C-terminal to the p7/NS2 junction; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
- Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 1b (Con1 strain)*

▪ APP159-- mCon1/JFHhRluc2(j5.1; 5 adapt muts (-E1E2))
- Special features: *chimeric junction within NS2; contains five adaptive mutations (confidential information) but lacks adaptive mutations with the envelope proteins; humanized Renilla luciferase reporter fused C-terminal to the p7/NS2 junction; JFH1 5'NTR, J6 3'NTR* (NOTE: JFH1 and J6 3'NTR differ only in variable region)
- Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 1b (Con1 strain)*

- *Bicistronic*

▪ APP109-- biCon1/JFHRluc1 (j5.1)
- Special features: *chimeric junction within NS2; Renilla luciferase reporter fused to N-terminal region of core; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
- Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 1b (Con1 strain); additional cell culture adaptation may be desirable*

▪ ***J4 strain***

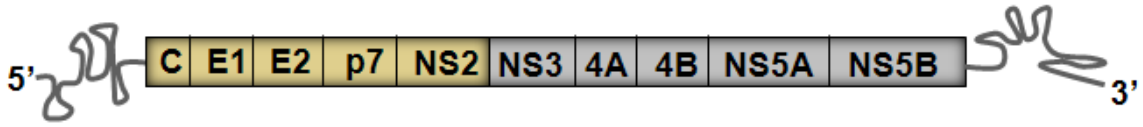
- Non-reporter
  - APP1032-- J4/JFH(j6; F886L, Q1496L)
    - Special features: *chimeric junction between NS2 and NS3; adaptive mutations within NS2 (F886L) and NS3 (Q1496L)*

- Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 1b (J4 strain)*

- Reporter
  - *Monocistronic*
    - APP1060-- mJ4/JFHhRluc3(j6; del, 2 adapt muts)
      - Special features: *chimeric junction between NS2 and NS3; two adaptive mutations (confidential information); Renilla luciferase reporter within domain III of NS5A; deletion within NS5A*
      - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 1b (J4 strain)*

- Heterologous NS5A
  - *APP1120-- J4/JFH(j6; 3 adapt muts; J4^{NS5A})*
    - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from J4 strain; contains three adaptive mutations (confidential information)*
    - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- **Genotype 2a/2a** ***(shown below with chimeric junction located between NS2 and NS3 (i.e. j6))***



  - ***J6 strain***

- Non-reporter
  - APP23-- J6/JFH (j5.1)
    - Special features: *chimeric junction within NS2; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
    - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 2a (J6 strain)*

  - APP21—J6/JFH (j6)
    - Special features: *chimeric junction between NS2 and NS3; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
    - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 2a (J6 strain)*

- Reporter
  - *Monocistronic*
    - APP24-- mJ6/JFHRluc2 (j5.1)

- Special features: *chimeric junction within NS2; Renilla luciferase reporter fused C-terminal to the p7/NS2 junction; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
- Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 2a (J6 strain)*

- APP150-- mJ6/JFHnsGluc2 (j5.1; S844G, R845Q, F846C)
  - Special features: *chimeric junction within NS2; Gaussia luciferase reporter fused C-terminal to the p7/NS2 junction*
  - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Gaussia luciferase readout), identification of entry inhibitors of genotype 2a (J6 strain)*

- APP22-- mJ6/JFHRluc2 (j6)
  - Special features: *chimeric junction between NS2 and NS3; Renilla luciferase reporter fused C-terminal to the p7/NS2 junction; JFH1 5'NTR, J6 3'NTR (NOTE: JFH1 and J6 3'NTR differ only in variable region)*
  - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 2a (J6 strain)*

- APP1061-- mJ6/JFHhRluc3(j6; del)
  - Special features: *chimeric junction between NS2 and NS3; Renilla luciferase reporter within domain III of NS5A; deletion within NS5A*
  - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 2a (J6 strain)*

- Heterologous NS5A
  - APP1105-- J6/JFH(j6; $H77^{NS5A}$)
    - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from H77 strain*
    - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

  - APP1106-- J6/JFH(j6; TN^{NS5A})
    - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from TN strain*
    - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

  - APP1107-- J6/JFH(j6; 1 adapt mut; $J4^{NS5A}$)
    - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from J4 strain; contains one adaptive mutation (confidential information)*
    - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

  - APP1108-- J6/JFH(j6; 2 adapt muts; $J4^{NS5A}$)
    - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from J4 strain; contains two adaptive mutations (confidential information)*

- Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- APP1109-- J6/JFH(j6; 1 adapt mut; $J6^{NS5A}$)
  - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from J6 strain; contains one adaptive mutation (confidential information)*
  - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- APP1110-- J6/JFH(j6; 1 adapt mut; $S52^{NS5A}$)
  - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from S52 strain; contains one adaptive mutation (confidential information)*
  - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- APP1111-- J6/JFH(j6; 2 adapt mut; $S52^{NS5A}$)
  - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from S52 strain; contains two adaptive mutations (confidential information)*
  - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- APP1112-- J6/JFH(j6; 4 adapt mut; $S52^{NS5A}$)
  - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from S52 strain; contains four adaptive mutations (confidential information)*
  - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- APP1113-- J6/JFH(j6; 3 adapt muts; $ED43^{NS5A}$)
  - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from ED43 strain; contains three adaptive mutations (confidential information)*
  - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- APP1114— J6/JFH(j6; 1 adapt mut; $SA13^{NS5A}$)
  - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from SA13 strain; contains one adaptive mutation (confidential information)*
  - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

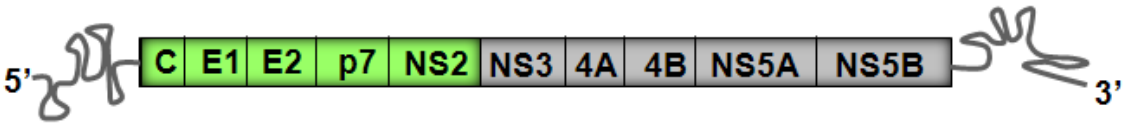
- APP1115— J6/JFH(j6; 2 adapt muts; $SA13^{NS5A}$)
  - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from SA13 strain; contains two adaptive mutations (confidential information)*
  - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- APP1116— J6/JFH(j6; 1 adapt mut; $NK6a^{NS5A}$)
  - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from NK6a strain; contains one adaptive mutation (confidential information)*

- Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- APP1117— J6/JFH(j6; QC69^{NS5A})
  - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from QC69 strain*
  - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- **Genotype 2b/2a** ***(shown below with chimeric junction located between NS2 and NS3 (i.e. j6))***

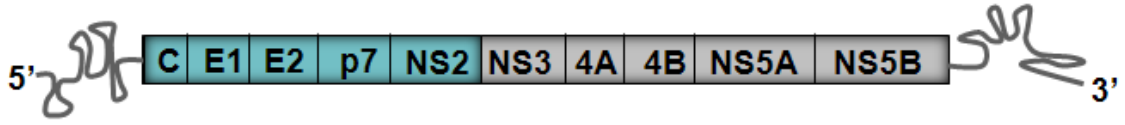


  - ***J8 strain***

    - Non-reporter
      - APP1033-- J8/JFH(j6)
        - Special features: *chimeric junction between NS2 and NS3*
        - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 2b (J8 strain)*

    - Reporter
      - *Monocistronic*
        - APP1062-- mJ8/JFHhRluc3(j6; del)
          - Special features: *chimeric junction between NS2 and NS3; Renilla luciferase reporter within domain III of NS5A; deletion within NS5A*
          - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 2b (J8 strain)*

- **Genotype 3a/2a** ***(shown below with chimeric junction located between NS2 and NS3 (i.e. j6))***



  - ***S52 strain***

    - Non-reporter
      - APP1035-- S52/JFH(j6; K1404Q)
        - Special features: *chimeric junction between NS2 and NS3; adaptive mutation wtihin NS3 (K1404Q)*
        - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 3a (S52 strain)*

      - APP1034-- S52/JFH(j6; I793S, K1404Q)
        - Special features: *chimeric junction between NS2 and NS3; adaptive mutations within p7 (I793S) and NS3 (K1404Q)*

- Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 3a (S52 strain)*

- APP1036-- S52/JFH(j6; I793S, S2274P)
  - Special features: *chimeric junction between NS2 and NS3; adaptive mutations within p7 (I793S) and NS5A (*S2274P*)*
  - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 3a (S52 strain)*

- Reporter

  - *Monocistronic*
    - APP1063-- mS52/JFHhRluc3(j6; del, 2 adapt muts)
      - Special features: *chimeric junction between NS2 and NS3; two adaptive mutations (confidential information); Renilla luciferase reporter within domain III of NS5A; deletion within NS5A*
      - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 3a (S52 strain)*

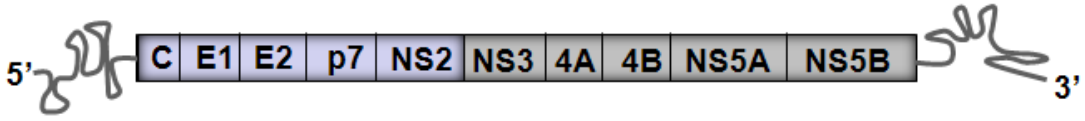
- Heterologous NS5A
  - APP1121-- S52/JFH(j6; 3 adapt muts; S52^{NS5A})
    - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from S52 strain; contains three adaptive mutations (confidential information))*
    - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- ***DBN strain***

- Non-reporter
  - APP1037-- DBN/JFH(j6; T1096A)
    - Special features: *chimeric junction between NS2 and NS3; adaptive mutation wtihin NS3 (*T1096A*)*
    - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 3a (DBN strain)*

  - APP1038-- DBN/JFH(j6; 2 adapt muts)
    - Special features: *chimeric junction between NS2 and NS3; adaptive mutations wtihin NS2 (W844R) and NS3 (K1404Q)*
    - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 3a (DBN strain)*

- **Genotype 4a/2a** ***(shown below with chimeric junction located between NS2 and NS3 (i.e. j6))***



- ***ED43 strain***

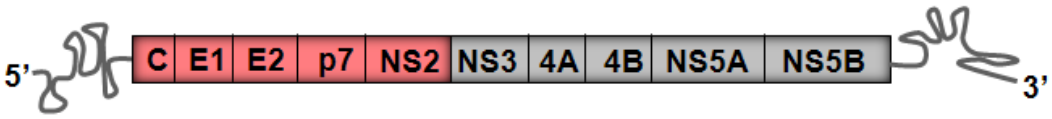
  - Non-reporter
    - APP1039-- ED43/JFH(j6; T827A, T977S)
      - Special features: *chimeric junction between NS2 and NS3; adaptive mutations wtihin NS2 (T827A and T977S)*
      - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 4a (ED43 strain)*

  - Reporter

    - *Monocistronic*
      - APP1064-- mED43/JFHhRluc3(j6; del, 2 adapt muts)
        - Special features: *chimeric junction between NS2 and NS3; two adaptive mutations (confidential information); Renilla luciferase reporter within domain III of NS5A; deletion within NS5A*
        - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 4a (ED43 strain)*

  - Heterologous NS5A
    - APP1122-- ED43/JFH(j6; 4 adapt muts; ED43^{NS5A})
      - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from ED43 strain; contains four adaptive mutations (confidential information))*
      - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- **Genotype 5a/2a** ***(shown below with chimeric junction located between NS2 and NS3 (i.e. j6))***



- ***SA13 strain***

  - Non-reporter
    - APP1040-- SA13/JFH(j6; A1022G, K1119R)
      - Special features: *chimeric junction between NS2 and NS3; adaptive mutations wtihin NS2 (A1022G) and NS3 (K1119R)*
      - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 5a (SA13 strain)*

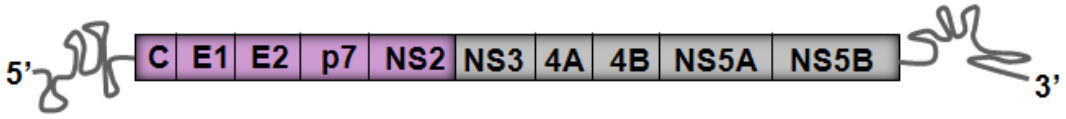
  - Reporter

    - *Monocistronic*
      - APP1065-- mSA13/JFHhRluc3(j6; del, 2 adapt muts)
        - Special features: *chimeric junction between NS2 and NS3; two adaptive mutations (confidential information); Renilla luciferase reporter within domain III of NS5A; deletion within NS5A*

- Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 5a (SA13 strain)*

- Heterologous NS5A
  - APP1123-- SA13/JFH(j6; 4 adapt muts; SA13^{NS5A})
    - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from SA13 strain; contains four adaptive mutations (confidential information))*
    - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- **Genotype 6a/2a** ***(shown below with chimeric junction located between NS2 and NS3 (i.e. j6))***



  - ***HK6a strain***

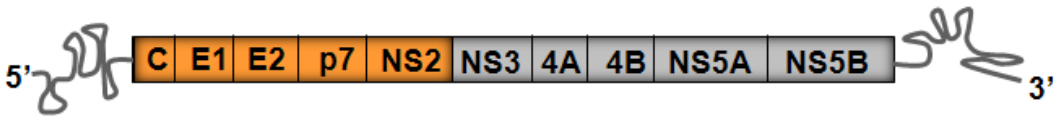
    - Non-reporter
      - APP1041-- HK6a/JFH(j6; F350S, N417T)
        - Special features: *chimeric junction between NS2 and NS3; adaptive mutations wtihin E1 (F350S) and E2 (N417T)*
        - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 6a (HK6a strain)*

    - Reporter

      - *Monocistronic*
        - APP1066-- mHK6a/JFHhRluc3(j6; del, 2 adapt muts)
          - Special features: *chimeric junction between NS2 and NS3; two adaptive mutations (confidential information); Renilla luciferase reporter within domain III of NS5A; deletion within NS5A*
          - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 6a (HK6a strain)*

      - Heterologous NS5A
        - APP1124-- HK6a/JFH(j6; 3 adapt muts; HK6a^{NS5A})
          - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from HK6a strain; contains three adaptive mutations (confidential information))*
          - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

- **Genotype 7a/2a** ***(shown below with chimeric junction located between NS2 and NS3 (i.e. j6))***



- *QC69 strain*
  - Non-reporter
    - APP1042-- QC69/JFH(j6)
      - Special features: *chimeric junction between NS2 and NS3*
      - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 7a (QC69 strain)*
    - APP1043-- QC69/JFH(j6; V17F, I414T)
      - Special features: *chimeric junction between NS2 and NS3; adaptive mutations within core (V17F) and E2 (I414T)*
      - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 7a (QC69 strain)*
    - APP1044-- QC69/JFH(j6; L882P, A2694V)
      - Special features: *chimeric junction between NS2 and NS3; adaptive mutations within NS2 (L882P) and NS5B (A2694V)*
      - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (RNA readout), identification of entry inhibitors of genotype 7a (QC69 strain)*
  - Reporter
    - *Monocistronic*
      - APP1067-- mQC69/JFHhRluc3(j6; del, 2 adapt muts)
        - Special features: *chimeric junction between NS2 and NS3; two adaptive mutations (confidential information); Renilla luciferase reporter within domain III of NS5A; deletion within NS5A*
        - Potential uses: *high throughput screening for inhibitors of all aspects of viral life cycle (Renilla luciferase readout), identification of entry inhibitors of genotype 7a (QC69 strain)*
  - Heterologous NS5A
    - APP1125-- QC69/JFH(j6; 1 adapt mut; $QC69^{NS5A}$)
      - Special features: *chimeric junction between NS2 and NS3; contains heterologous NS5A from QC69 strain; contains one adaptive mutation (confidential information)*
      - Potential uses: *screen for genotype-specific NS5A inhibitors, evaluate genotype specificity of existing NS5A inhibitors*

PERMISSIVE CELL LINES

- APC49—Huh7.5-- cell line that is highly permissive to HCV replication; derived by "curing" replicon cell line via Interferon treatment
- APC167 Huh7.5.1-- cell that that was generated by "curing" replicon-containing Huh7.5 cells
- APP170—Huh7.5.1 clone 2-- cell that that was generated by "curing" replicon-containing Huh7.5.1 cells